Fear Conditioning and Affective Modulation of the Startle Reflex in Male Adolescents with Early-Onset or Adolescence-Onset Conduct Disorder and Healthy Control Subjects

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Background: Impairments in emotional processing may play an etiological role in the development of aggressive or antisocial behavior such as is seen in conduct disorder (CD). These findings may be developmentally sensitive, with neuropsychological impairments confined to those with the early-onset form of CD, which emerges in childhood. We investigated whether adolescents with early- or adolescence-onset CD would acquire fear conditioned responses to a visual conditioned stimulus and show a normal pattern of affective modulation of the startle reflex.

Methods: Electrodermal activity was measured during the fear conditioning process, and electromyographic recording methods were used to assess blink magnitudes elicited by acoustic startle probes during the viewing of emotionally valenced pictures. Forty-one early-onset CD, 28 adolescence-onset CD, and 54 healthy control adolescents participated in the study.

Results: Both CD groups showed impaired differential fear conditioning relative to control subjects, while retaining the ability to generate normal skin conductance responses to the aversive unconditioned stimulus. There was a similar relationship between emotional valence of the slides and startle magnitude in CD and control adolescents, but startle-elicited blinks were lower across all emotion categories in both CD subtypes.

Conclusions: Fear conditioning deficits and reduced startle amplitudes were observed in participants with early- and adolescence-onset forms of CD. These findings are consistent with impairments in neural systems subserving emotion and involving the amygdala in CD, regardless of age of onset.

Key Words: Aggression, amygdala, antisocial behavior, conduct disorder, fear conditioning, startle

Conduct disorder (CD) is characterized by a persistent pattern of serious aggressive and antisocial behavior and a disregard for the rights of others (1). Moffitt (2) suggested that individuals with CD can be divided into those with an early-onset or life-course persistent form of the disorder and those with an adolescence-limited form. The former, early-onset group show verbal intelligence quotient (IQ) deficits and associated neurodevelopmental difficulties. In contrast, the adolescence-limited group are thought to lack significant neuropsychological impairment, and their antisocial behavior is considered to arise due to peer group processes. The developmental taxonomic theory of CD (2) therefore predicts that any neurobiological or neuropsychological differences observed between healthy adolescents and those with CD should be largely confined to those with the early-onset form.

It has been argued that emotional processing may be disrupted in individuals with persistent antisocial behavior (such as is found in CD) and that this is causally related to the etiology of the condition (3). Impairments in emotional processing may arise due to deficits in a neural system involving the amygdala. Deficient amygdala activation has been reported during the viewing of affective pictures in clinical cases with early-onset CD (4). The amygdala is critically involved in emotional learning (5). Lesion studies have shown that the amygdala is required for the acquisition of fear conditioned responses (6,7) and neuroimaging studies in humans have confirmed that the amygdala is activated during fear conditioning (8). Accordingly, we examined conditioning ability in adolescents with early- and adolescence-onset CD, as this may represent a peripheral measure of amygdala function.

We also examined affective modulation of the eye-blink startle reflex, since a recent report suggested that the startle reflex to an acoustic probe was attenuated in children with oppositional defiant disorder (ODD) (9), a precursor of CD (10). An aberrant pattern of affective modulation has been reported in adult psychopaths (11,12). As such, we determined whether adolescents with CD would show patterns of affective modulation consistent with findings from ODD children or adult psychopaths. Individuals high in psychopathic traits also show reduced psychophysiological responses to visual stimuli connoting distress relative to those connoting threat (11,13). These findings have been interpreted in terms of a model of reduced empathy (13) or as reflecting impairment of the defensive motivational system (11). Therefore, a further aim of the study was to examine startle modulation by different classes of negatively valenced pictures.

The objectives of this study were to investigate fear conditioning and affective modulation of the startle reflex in adolescents with early- or adolescence-onset CD and age-matched control subjects with no lifetime history of antisocial behavior. Based on the developmental taxonomic theory (2), our primary hypothesis was that the early-onset subgroup would show impairment relative to control subjects. The possibility of emo-

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tional dysfunction in adolescence-onset CD remained open but was of theoretical and clinical significance given that the prognosis for this subgroup is also unfavorable (14).

Methods and Materials

Participants

The sample consisted of male adolescents aged between 14 and 18 years. Participants were recruited from secondary schools and further education colleges in relatively deprived areas of Cambridge, pupil referral units for teenagers who had been permanently excluded from mainstream schools, and the Youth Offending Service. Socioeconomic status (SES) was categorized according to the National Statistics Standard Occupational Classification 2000 guidelines. Diagnostic interviews using the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (Kiddie-SADS-PL) instrument (15), which reflects DSM-IV criteria, were carried out with all participants and their main caregiver to screen for current and lifetime psychopathology. This process yielded 54 healthy control subjects (HCs) with no lifetime history of serious antisocial behavior and no current psychiatric illness and 71 adolescents with CD, of whom 43 were classified as having early-onset CD (EO-CD) and 28 were classified as having adolescence-onset CD (AO-CD). Written informed consent was provided by all participants.

Exclusion criteria for participation were IQ < 75 as estimated using the Block Design and Vocabulary subtests of the Wechsler Abbreviated Scale of Intelligence (16), presence of autistic spectrum or pervasive developmental disorder, presence of chronic physical illness, and current use of steroid medication.

Participants were allocated to the EO-CD group if they or their caregiver reported at least one CD symptom and functional impairment was present prior to the age of 10 years or if they met full criteria for ODD before age 10 and developed CD after the age of 10. Inclusion in the study was based on lifetime diagnoses of CD, although the majority (92%) of index cases had a current CD diagnosis at the time of testing.

Ten participants with EO-CD and four with AO-CD had current comorbid attention-deficit/hyperactivity disorder (ADHD). All participants with ADHD had been medication-free for at least 6 months. One AO-CD and five EO-CD participants received a comorbid diagnosis of major depressive disorder (MDD). Six HC, four EO-CD, and two AO-CD participants had past MDD. Finally, one participant with AO-CD had comorbid generalized anxiety disorder and one EO-CD participant was taking fluoxetine at the time of testing.

Skin Conductance Recording

Electrodermal activity was measured using the MP150 system and a skin conductance level amplifier (GSR100C) and transducer (TSD203) (all BIOPAC Systems, Inc., Goleta, California) at a rate of 100 Hz. The electrodes of the transducer were filled with skin conductance paste and attached to the distal phalanges of the index and middle fingers of the nondominant hand. The task computer sent digital markers to the MP150 system to indicate slide onset and offset and onset of the white noise probe in additional recording channels. Data were analyzed offline using AcqKnowledge 3.7.2 (BIOPAC Systems, Inc.).

Skin Conductance Response Conditioning

The fear conditioning procedure used differential conditioning (conditioned stimulus [CS]+ = blue slides and CS− = red slides) with partial reinforcement (the CS+ was reinforced 10 times and unreinforced 8 times during acquisition) following Bechara and Damasio (17). Briefly, we used monochrome slides as the visual conditioned stimuli, a loud (99 dB) and aversive white-noise tone lasting 1000 msec as the unconditioned stimulus (US), and the amplitude of the skin conductance response (SCR) in the 7 sec period following CS+ presentation as the dependent measure of the conditioning process (see 17 for further details). The colored slides were presented for 3 sec each with a 10 sec interslide interval. The aversive tone was presented binaurally via headphones. When presented with the CS+, the onset of the white-noise tone was 2 sec after slide onset. Quantification of conditioned SCR amplitude within the 7 sec analysis window was achieved using the peak-to-peak function in AcqKnowledge and the slope function to determine the direction of the change. A positive amplitude exceeding .1 μS was considered to indicate an elicited SCR, although values used in the statistical analyses and shown in Figure 1 reflect absolute changes in skin conductance level (SCL) within the 7 sec analysis window.

The habituation phase (HAB) involved two presentations of the CS+ and the CS−, interspersed with other colored slides. The acquisition phase was divided into acquisition 1 (ACQ1, comprising the first four unreinforced CS+, five reinforced CS+, and five presentations of the CS+) and acquisition 2 (ACQ2, in which the same combination of slides were presented in a different order). Extinction (EXT) involved presenting the CS+ six times without reinforcement and the CS− a further three times. The average change in SCL in response to each CS type (CS+ unreinforced, CS+ reinforced, or CS−) during a given learning phase was quantified. For the analysis of differential conditioning, only changes related to CS+ unreinforced and CS− were considered.

To control for differences in attention, a memory test was performed following the experiment that involved asking the participant to recall how many colors they had seen (a score of .5 for correct answer) and to name the colors in question (.5 for each correct answer). They were also asked to name the number of slides paired with the aversive sound (.5 for correct answer) and the color of the slide that had been paired with the aversive sound (2.0 for correct answer; 1.0 if they said blue and red/another color).

Affective Modulation of the Startle Reflex

We modified the design employed by Patrick *et al.* (12) to disaggregate responses to different classes of emotionally valenced slides. Each participant viewed a series of 45 slides depicting 9 positive (POS), 9 neutral (NEU), 9 sad slides (SAD), 9 disgust slides (DIS), and 9 fear slides (FEAR), all taken from the International Affective Pictures System (IAPS) (18; see Table 1 for normative valence and arousal ratings for adults and Appendix 1 for relevant slide numbers). Slides were presented in a fixed, pseudo-random sequence, with the order identical for all participants. Each slide was displayed for 10 sec with an interslide interval of 10 sec.

Eye-blink responses to the startle probes were measured using silver/silver chloride (Ag/AgCl) electrodes positioned over the orbicularis oculi muscle below the left eye, according to established guidelines (19). Electromyographic (EMG) data were recorded at a rate of 1000 Hz using an EMG100C amplifier module (BIOPAC Systems, Inc.), with a bandpass of 30 to 500 Hz. A 99 dB white-noise probe lasting 100 msec was presented binaurally via headphones. To reduce the impact of habituation, only 30 of the slides were accompanied by the startle probe (6 of 9 slides from each category). The slides were presented in blocks

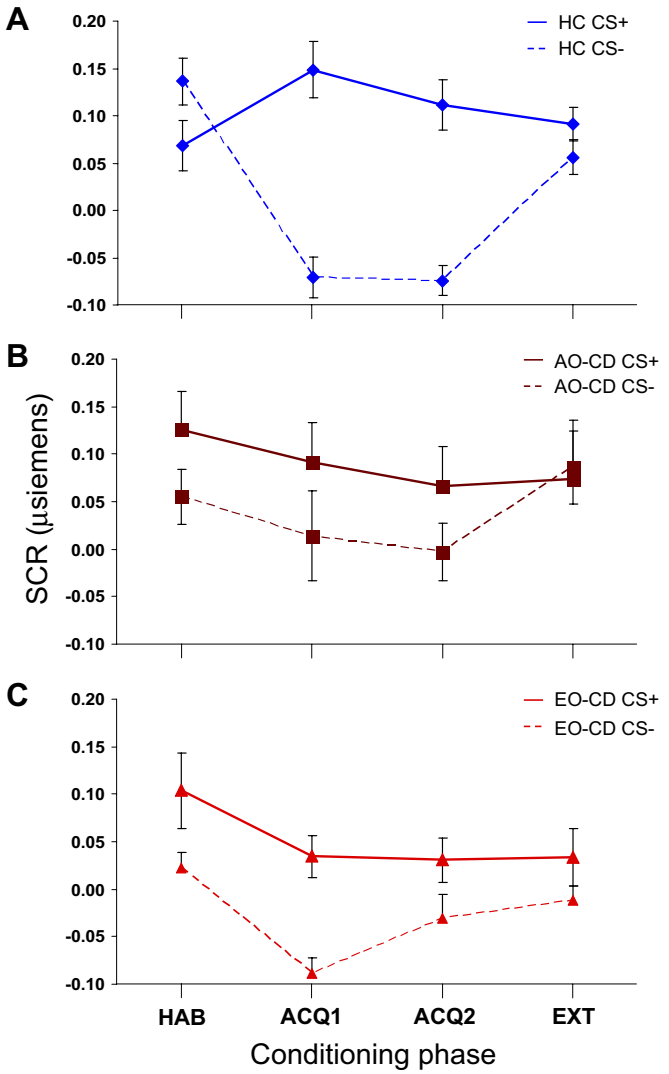

Figure 1. Mean (± SE) skin conductance responses to blue test slides (CS+, solid line) and red slides (CS−, dashed line) across conditioning phases, in **(A)**: HC, **(B)**: AO-CD, and **(C)**: EO-CD groups. Only the HC group shows any evidence of differential conditioning as shown by the fact that SCR values for CS+ and CS− cross over between HAB and ACQ1 phases and the marked difference between these values at ACQ1 and ACQ2. ACQ1, acquisition 1 (comprising the first four unreinforced CS+, five reinforced CS+, and five presentations of the CS+); ACQ2, acquisition 2 (the same combination of slides were presented as in acquisition 1 but in a different order); AO-CD, adolescence-onset conduct disorder; CS, conditioned stimulus; EO-CD, early-onset conduct disorder; EXT, extinction phase; HAB, habituation phase; HC, healthy control subjects; SCR, skin conductance response.

to examine possible effects of habituation. Probe presentation occurred 2.5, 3.5, or 4.5 sec after slide onset.

Startle responses were quantified offline using the AcqKnowledge functions Max and Min in the EMG channel using an analysis window that began 30 msec after startle probe onset and terminated 100 msec after onset. These values were subtracted from baseline Max and Min values within the 50 msec period prior to probe onset to yield an integrated value for startle amplitude, expressed in analog-to-digital (A/D) units.

Data Analyses

Due to technical problems, startle data were only available for 50 HC, 39 EO-CD, and 25 AO-CD participants, and fear conditioning data were only available for 50 HC, 41 EO-CD, and 26 AO-CD participants.

To examine possible demographic differences, one-way analysis of variance (ANOVA) or chi-square tests were used. Nonnormal data were square-root transformed. Repeated-measures ANOVAs were performed with diagnostic group as a between-subjects factor and either conditioning phase or slide valence as a within-subjects factor. Where the assumption of sphericity was violated, degrees of freedom were corrected using Greenhouse-Geisser or Huynh-Feldt estimates of sphericity as appropriate (20). Dependent measures were SCR amplitudes at each conditioning phase or startle reflex magnitudes to each slide valence. Tukey Honestly Significant Difference (HSD) tests were used to perform post hoc contrasts. Analyses were conducted using SPSS 11.5 (SPSS Inc., Chicago, Illinois).

Results

Demographic Information

The participants' demographic and diagnostic data are summarized in Table 2. There was a significant group effect for estimated IQ [$F(2,122) = 18.68$, $p < .001$]. Post hoc comparison showed that mean IQ was lower in both CD groups relative to HC ($p = .01$ and $p < .001$, respectively, for AO-CD and EO-CD groups). The EO-CD group was of lower SES than the HC group [$\chi^2(2) = 22.9$, $p < .001$]. Analysis of the ethnicity data (using categories of white or other) showed that the EO-CD group contained fewer nonwhite participants than the AO-CD group [$\chi^2(1) = 8.7$, $p < .005$]. There was a significant group effect for CD symptoms [$F(2,122) = 233.84$, $p < .001$]; post hoc comparison showed that both CD groups had more symptoms than HC (both $p < .001$), and EO-CD participants had more symptoms than AO-CD participants ($p < .001$).

Fear Conditioning

All participants achieved a recall score of at least 1.5 out of 5, so none were excluded from subsequent analyses (17). The mean recall scores for each group (± SD) were as follows: HC = 4.53 (± .79), AO-CD = 4.52 (± .67), and EO-CD = 4.05 (± .91). Although there was a main effect of group [$F(2,114) = 4.55$, $p < .05$], the fact that the mean scores were relatively high suggests that group differences in fear conditioning performance were not due to a failure to pay attention to the task.

There was a main effect of group on SCL values at baseline, prior to onset of the first visual stimulus [$F(2,116) = 5.81$, $p < .01$;

Table 1. Mean (± SE) Normative Valence and Arousal Ratings for the Five Slide Categories

Slide Category	Valence[a]	Arousal[b]
Positive	7.29 (± .60)	5.47 (± .64)
Neutral	5.04 (± .31)	2.64 (± .49)[c]
Sad	2.65 (± .53)	4.87 (± .64)[d]
Disgust	2.51 (± .68)	5.97 (± .94)
Fear	3.70 (± .77)	6.30 (± .86)

[a]Where 1 = most negative and 9 = most positive valence possible; main effect of valence [$F(4,44) = 99.52$, $p < .001$]; post hoc comparison showed differences between all slide categories, except for Disgust and Sad slides, which were of equal valence.

[b]Where 1 = lowest arousal and 9 = highest arousal possible; main effect of arousal [$F(4,44) = 35.22$, $p < .001$].

[c]$p < .01$ relative to all other slide categories.

[d]$p < .05$ relative to disgust and fear.

Table 2. Demographic Characteristics

	HC (n = 54)	AO-CD (n = 28)	EO-CD (n = 43)
Age	15.84 ± .89	15.62 ± .86	15.88 ± .87
IQ	106.87 ± 11.92	99.07 ± 11.25	92.79 ± 10.59
CD Symptoms	.2 ± .6	6.4 ± 2.0	8.5 ± 2.9
SES			
Low	5 (9.3%)	7 (25.0%)	17 (39.5%)
Middle	10 (18.5%)	8 (28.6%)	12 (27.9%)
High	36 (66.7%)	12 (42.9%)	8 (18.6%)
Ethnicity			
White	49 (90.7%)	21 (75.0%)	42 (97.7%)
Mixed-race	2 (3.7%)	4 (14.4%)	1 (2.3%)
Black	2 (3.7%)	1 (3.6%)	
Asian	1 (1.9%)	1 (3.6%)	
Mediterranean		1 (3.6%)	

Data are presented as means ± SD or number and percentage in each subgroup.

Please note SES information was not available for 3 HC, 1 AO-CD, and 6 EO-CD participants.

AO-CD, adolescence-onset conduct disorder; CD, conduct disorder; EO-CD, early-onset conduct disorder; HC, healthy control subjects; IQ, intelligence quotient; SES, socioeconomic status.

Table 3); post hoc comparison showed that values were lower for the AO-CD group relative to HC ($p < .005$).

Although there was a significant habituation effect on SCRs to the unconditioned stimuli [$F(3.73,424.78) = 70.65$, $p < .001$], there was no main effect of group [mean (± SD) values in μS for HC = .85 (± .64), AO-CD = 1.05 (± .99), and EO-CD = .73 (± .70); $F(2,114) = 1.76$, $p = .18$]. This suggests that the US was experienced as equally aversive by each experimental group.

We examined the possibility of group differences in conditioning ability using a group × phase × CS type (CS+ vs. CS−) mixed-model ANOVA to assess whether the relationship between learning phase and CS type was affected by group status. This revealed a significant three-way interaction [$F(6,798) = 5.37$, $p < .001$], which appeared to be accounted for by the fact that CS+ and CS− SCR values cross over between HAB and ACQ1 in the HC group only. The magnitude of the SCR difference between the CS+ and CS− was also greater at ACQ1 and ACQ2 in HCs relative to the CD groups (Figure 1). We explored this further by performing separate repeated-measures ANOVA tests for each CS type. For the CS+ (unreinforced blue slide), we found no effect of phase [$F(2.91,332.05) = 1.22$, $p = .30$] or group [$F(2,114) = 1.56$, $p = .21$] but a significant group × phase interaction [$F(5.83,332.05) = 2.16$, $p < .05$]. This showed that the SCR to the CS+ differed across learning phases in the HC group, relative to both CD subgroups, as shown by the increase in SCR between HAB and ACQ1 in HC participants only. For the CS− (red slide), there was a main effect of phase [$F(2.75,313.19) = 23.70$, $p < .001$] and group [$F(2,114) = 3.71$, $p < .05$] and a significant group × phase interaction [$F(5.49,313.19) = 4.95$, $p < .001$]. This indicated that the SCR to the CS- also differed across learning phases in HCs, relative to participants with both CD subtypes. As such, the data suggest that both processes involved in differential conditioning (what may be termed "fear learning" to the CS+ and "safety learning" to the CS−) were abnormal in CD.

Estimated IQ, SES, ethnicity, age, ADHD diagnoses, symptom counts for ADHD, and recall score were not found to be significant covariates of conditioning ability.

Startle Reflex Modulation

Data from seven participants (three HC, three AO-CD, and two EO-CD) were excluded from further analysis because they showed mean startle amplitudes <25 A/D units (21). Although raw values are reported below and presented in Figures 2 and 3, all subsequent analyses were performed using square-root transformed data.

Habituation

We first examined potential habituation effects by assessing whether blink magnitudes decreased over time and, if so, whether this differed according to diagnostic group. Figure 2 shows the changes in blink response magnitude across the six blocks containing a neutral slide paired with a startle probe. A repeated-measures ANOVA revealed a main effect of time [$F(5,515) = 25.75$, $p < .001$] and group [$F(2,103) = 11.46$, $p < .001$] but no group × time interaction. Post hoc comparison showed that both CD groups differed from HC (both $p < .001$). This suggests that habituation occurred in a parallel fashion in all three groups but that the CD groups' blink amplitudes were consistently lower when viewing neutral slides. The pattern of habituation showed both a linear trend [$F(1,103) = 57.22$, $p < .001$] and a quadratic trend [$F(1,103) = 50.94$, $p < .001$].

Effect of Affective Modulation

There was a clear effect of slide valence on startle response amplitudes: viewing positive slides resulted in lower blink amplitudes relative to the other four slide types [effect of valence: $F(4,412) = 19.79$, $p < .001$]. The mean values (± SD) for each emotion category were as follows: POS = 152.36 (± 135.08), NEU = 181.83 (± 153.45), SAD = 184.08 (± 155.84), DIS = 196.97 (± 162.20), and FEAR = 186.90 (± 153.53). Post hoc comparisons confirmed that blinks were smaller when viewing positive slides, relative to all other slide types (all $p < .001$). In addition, blink amplitude when viewing disgust slides differed from all other slide types (DIS > POS, NEU, SAD, and FEAR, $p < .05$ or less). Effect sizes for comparisons between POS and the other slide types were small (22); all other comparisons yielded negligible effect sizes.

Group Differences

There was a main effect of group on startle magnitude [$F(2,103) = 12.81$, $p < .001$]; post hoc comparison showed that both CD groups differed from control subjects (both $p < .001$ relative to HC; $d = -1.00$ and $-.76$ for AO-CD and EO-CD, respectively), but there was no difference between the CD groups ($p = .33$; Figure 3). Thus, both CD groups showed attenuated blink amplitudes, a pattern that held across all five emotion categories. There was no interaction between slide valence and diagnostic group; therefore, both CD groups appeared to show similar patterns of affective modulation to control subjects.

Estimated IQ, SES, age, and symptom counts for ADHD and CD were not found to be significant covariates of startle reflex

Table 3. Baseline Skin Conductance Levels by Group

Experimental Group	Baseline SCL (± SE)
HC	7.59 (± .39)
AO-CD	5.48 (± .44)[a]
EO-CD	6.58 (± .41)

AO-CD, adolescence-onset conduct disorder; EO-CD, early-onset conduct disorder; HC, healthy control subjects; SCL, skin conductance level.

[a]Significantly lower than HC ($p < .005$).

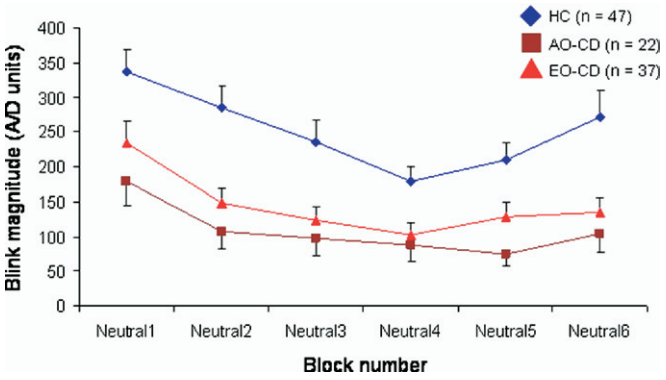

Figure 2. Effect of habituation on startle response magnitudes to the startle probe when viewing neutral slides, according to diagnostic group status.

modulation. Ethnicity was a significant covariate ($p < .05$), with ethnic minority participants having lower startle magnitudes. After controlling for ethnicity, the group effect remained significant ($p < .001$).

Discussion

Compared with healthy control subjects, adolescents with both forms of CD showed impaired differential fear conditioning and attenuation of the eye-blink startle reflex to an acoustic probe when viewing affective pictures. The lack of differences in conditioning or emotion processing between the AO-CD and EO-CD groups suggests similar emotional impairment in both subtypes. These findings are the first to be obtained in this age range using a relatively large community sample with acceptable power to detect main effects of group and follow in the tradition of pioneering work in adult psychopaths (23,24).

Participants from both CD subgroups were able to generate SCRs to the primary US, suggesting a selective deficit in emotional learning. They were also aware of the CS+ -US contingency, indicating that the conditioning deficits observed were not the result of cognitive learning impairments. Interestingly, the CD participants appeared to show deficits in separate aspects of autonomic conditioning; these may be termed fear learning to the CS+ and safety learning to the CS−. In addition to a failure to exhibit an increase in SCRs to the CS+ between the HAB and ACQ1 learning phases, they showed a less marked decrease in SCRs to the CS− over the same period. As such, they demonstrated less effective autonomic discrimination between the respective CS types than control subjects. An earlier study reported a complex relationship between antisocial behavior and conditioning ability in a community sample of boys from different social classes (25). Poor conditioning was observed in high SES antisocial boys, whereas conditioning was actually enhanced in low SES antisocial boys relative to low SES control subjects. A follow-up of this sample found that individuals classified as antisocial during adolescence, but who had desisted from engaging in criminal activity in adulthood, showed enhanced conditioning relative to those classified as antisocial during adolescence and convicted of an offence in the intervening period (26). This suggests that intact or superior conditioning ability may act as a psychophysiological protective factor.

The present findings are consistent with the possibility that the neural substrates of fear conditioning, involving the amygdala, are impaired in CD, since patients with amygdala lesions show similar patterns of impairment on fear conditioning tasks (6,7). Neuroimaging studies in healthy volunteers demonstrate that the amygdala is recruited during the fear conditioning process (8), providing further support for this interpretation. A recent neuroimaging study in adult psychopaths reported deficient activity of the limbic-prefrontal circuit during fear conditioning (27). These data were collected in parallel with autonomic measures, which confirmed that the psychopaths failed to show conditioning. As such, there appears to be some similarity between our findings and those obtained with adult psychopaths.

The present findings also show attenuation of the eye-blink startle reflex in both CD groups relative to control subjects. The reduction in eye-blink magnitude was not emotion category-specific but, rather, was observed across all five slide categories. As such, there was no evidence for changes in the pattern of affective modulation itself, with adolescents of both CD subtypes showing a similar relationship between slide valence and blink magnitude to control subjects. Our findings are therefore consistent with a previous report showing attenuation of the startle reflex across emotional categories in children with ODD (9) but differ from findings in adult psychopaths who exhibit an aberrant pattern of affective modulation (11,12). Patients with amygdala lesions show reduced startle amplitudes in some (28,29) but not all studies (30). These individuals also show a lack of startle potentiation by aversive visual primes (28,31). Etiologically, our findings may reflect impairment of the brainstem circuitry that mediates the startle reflex (32) or a tonic reduction in amygdala output to this circuit (33).

We formed separate categories of sad, disgust, and fear slides rather than collapsing these together as a single negative category because previous studies in psychopaths have reported relative insensitivity to distress versus threat stimuli in startle and autonomic response patterns (11,13). These findings have been interpreted in terms of a model of reduced empathy, which is proposed to disrupt the socialization process (13). However, no evidence was found to support this distinction in participants from either CD subgroup.

Contrary to the predictions of the developmental taxonomic theory (2), we found comparable impairment in fear conditioning and startle reflex responses in both EO-CD and AO-CD groups. This suggests no etiological distinction between subtypes at the level of emotion processing as measured. From a neurobiological perspective, deficits in emotional learning or emotion processing can be interpreted as follows: 1) emotional

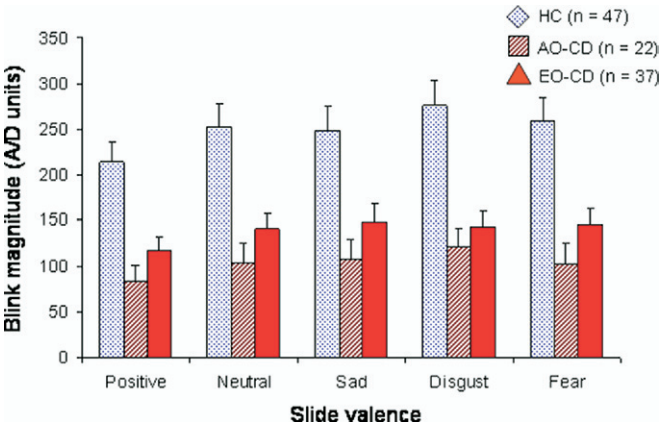

Figure 3. Effect of slide valence on mean startle magnitude, according to diagnostic group status.

dysfunction may have occurred as a consequence of chronically engaging in antisocial behavior; or 2) premorbid emotional dysfunction was present in both groups of CD adolescents, but other factors determined the timing of onset. For example, protective processes in the social environment such as authoritative parenting might conceivably delay the emergence of CD until adolescence in those with a biological vulnerability toward externalizing behavior. Alternatively, factors within the individual promoting resilience, such as intact executive functioning, may act to delay or prevent the onset of CD in those with emotional dysfunction. The present data do not allow us to distinguish between these possibilities.

Limitations and Strengths

There were several demographic differences between HC and CD groups, including a discrepancy in terms of SES. These differences did not appear to affect the results, and given earlier findings of enhanced conditioning in low SES antisocial adolescents (25), the SES difference might have been expected to obscure group effects.

It is possible that retrospective accounts may have classified some participants incorrectly in terms of CD onset, especially because the severity of the behavior problems shown by all participants with CD appeared to increase during adolescence. We attempted to circumvent this problem by asking informants about the onset of each CD and ODD symptom and treating ODD as a precursor of CD.

We found only limited startle potentiation by negative visual primes in control subjects (confined to disgust), which made it more difficult to assess affective modulation in CD. This may have been due to the high proportion of negative slides used in the study. Nevertheless, adolescents with CD do not appear to show an aberrant pattern of affective modulation similar to that seen in adult psychopaths.

In terms of strengths, we were able to recruit a relatively large sample of conduct-disordered participants. Our comprehensive psychiatric screening of participants for CD and comorbid diagnoses means that the groups were well defined in terms of current and lifetime psychiatric disorder. All participants were ascertained from the community (rather than clinics, psychiatric hospitals, or juvenile detention centers). Finally, the outcome measures employed were not readily influenced by motivational factors, as these may differ between participants with CD and healthy control subjects (34).

In conclusion, this is the first study to demonstrate deficits in fear conditioning and attenuation of the startle reflex in adolescents with CD. Furthermore, the data clearly show that these impairments are present to a similar degree in those with early- and adolescence-onset CD. This represents a challenge to current etiological theories, which suggest that neuropsychological and neurobiological factors play little or no role in the development of adolescence-onset CD.

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Appendix 1

The following were the 45 pictures employed, by International Affective Pictures System (IAPS) identification number: positive: 1440, 1710, 2352, 8190, 8380, 8461, 8490, 8496, 8531; neutral: 6150, 7000, 7002, 7006, 7009, 7080, 7090, 7140, 7150; sad: 2800, 2900, 3300, 9040, 9041, 9421, 9560, 9561, 9921; disgust: 3000, 3060, 3071, 3110, 3150, 3400, 9181, 9042, 9320; fear: 1050, 1201, 1280, 1300, 1931, 3500, 6244, 6260, 6370.