Brain Maturation and Subtypes of Conduct Disorder: Interactive Effects on P300 Amplitude and Topography in Male Adolescents

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ABSTRACT

Objective: Adolescents with conduct disorder problems are, on average, at increased risk for a variety of unfortunate adult outcomes, including substance dependence. This study was designed to identify the neurophysiological correlates of different categories of conduct disorder problems as well as the relationship between these correlates and the maturational status of the brain. Method: The subjects were 94 males, aged 14–19 years, recruited from the community. None were recruited from treatment or juvenile justice programs. The subjects varied in the type and number of conduct problem behaviors exhibited prior to age 15. Groups were operationally defined by the relative number (0 versus ≥1) of DSM-IV conduct disorder diagnostic criteria within each of four categories: rules violations, aggression, deceitfulness/theft, and destructiveness. Age was included as an additional grouping factor. P300 evoked electroencephalographic potentials were recorded while subjects performed a task in which rare auditory stimuli were used to signal a change in stimulus-response mapping during a succeeding set of trials. Results: Analyses revealed that boys with a history of rules violations failed to exhibit the normal maturational increase in P300 amplitude found in boys without a history of rules violations. Topographic analyses of current source densities suggest that the source of the maturational deficit involved P300 generators within the frontal brain. Parietal generators of P300 matured normally. Conclusions: The present results are interpreted as reflecting a decrement in frontal brain maturation among boys potentially at risk for substance dependence, antisocial personality disorder, or other forms of adult psychopathology. J. Am. Acad. Child Adolesc. Psychiatry, 2003, 42(1):106–115.

Key Words: conduct disorder, evoked potentials, brain maturation.
In a recent study, Hill and colleagues (1999) utilized the P300 to examine brain maturation among male and female children at higher versus lower risk for alcoholism. Risk was operationally defined by the presence of a family history of alcoholism. Of interest, an analysis of growth curves across the age range of 7–18 years showed that the quadratic function fit to auditory P300 amplitude increased at a slower rate among children in the high-risk group. The group difference in the quadratic relationship between auditory P300 amplitude and age was most reliably detected in males. Hill and colleagues did not examine the scalp topography of the group difference in P300 maturation.

In 1999, we (Bauer and Hesselbrock, 1999a) described a study of P300 data recorded from adolescents, aged 14–20 years, while they performed a visuospatial task. Via a cross-sectional analysis of the effects of aging, we replicated the common finding of an age-related reduction in visual P300 amplitude (Hill et al., 1999). This decline in visual P300 with age stands in juxtaposition to the equally common finding of an increase in auditory P300 with age, demonstrated by Hill et al. (1999) as well as other investigators (Ladish and Polich, 1989).

Our 1999 study examined the effects of differential risk for alcoholism defined by the presence of a severe level of conduct problem behaviors exhibited prior to age 15. Analyses of P300 voltages revealed that the effect of conduct problems on P300 amplitude was evident at posterior electrode sites among adolescents younger than 16.5 years. Among adolescents aged 17–20 years, the effect of conduct problems was most prominent at anterior sites. Thus the neuroanatomical correlate of conduct problems appeared to change with age.

The present study was designed to elaborate upon the hypothesis that the maturational status of the brain interacts with the location of the neurophysiological substrate(s) of conduct problem behaviors. More specifically, we were interested in determining whether advanced methods of P300 source localization—namely, current source densities (CSDs) calculated via the neuroanatomically constrained boundary element method (BEM) (Kristeva-Feige et al., 1997)—would yield a more precise map of maturational deficits than had been obtained in our 1999 analyses of raw P300 voltages.

A second goal of this study was to determine whether the relationship between P300 amplitude, conduct problems, and aging generalized to a newly developed auditory task that places high demands on response regulation. Previous research has shown that children with conduct problems perform poorly on neuropsychological tasks which measure the self-regulation of behavior (Daugherty and Quay, 1991; Shapiro et al., 1988). In the present study, it was hypothesized that adolescents with conduct problems would be less able to shift their response set when required by task instructions. It was predicted that this perseverative responding would be related to reduced P300 amplitude at frontal electrode sites (Kim et al., 2001).

The third goal was to examine the effects of subtypes of conduct problems and whether these subtypes would have different neurophysiological correlates. In a recent publication (Bauer and Hesselbrock, 1999b), we reported that P300 amplitudes, recorded while teenage subjects performed the Stroop color naming test, were more strongly related to the number of rules violations than to the number of aggression, deceitfulness/theft, or destructiveness CD criteria. In the present study, we hoped to replicate this finding and examine its topography using the CSD/BEM modeling techniques mentioned above.

METHOD

All procedures and documents associated with this research had undergone prior review and approval by the University of Connecticut Health Center’s Institutional Review Board. The research was conducted in compliance with the ethical standards described within the Helsinki Declaration and the Belmont Report.

Subjects

The subjects included in the data analysis were 94 males, 14 to 19 years old. Subjects were recruited via their parents’ response to newspaper advertisements or presentations at alcohol/drug treatment programs and support groups. Subjects were also recruited through guidance counselors and presentations before high school classes, YMCA/YWCA organizations, and police athletic leagues or similar organizations. Interested adolescents or their parents were invited to telephone a research assistant for additional information and screening.

Each subject and one of his parents were interviewed separately at the University of Connecticut Health Center. At the start of the interviews, the subject and parent provided written informed consent. Psychiatric histories were obtained from both the subject and parent via the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA). The SSAGA is a highly reliable (Bucholz et al., 1994) and valid (Hesselbrock et al., 1999) instrument that covers the major psychiatric disorders defined in the DSM and in other systems. DSM-IV criteria were applied to the information provided by the adolescent subjects and used for the ascertainment of CD and other major Axis I and Axis II disorders. A detailed family history was ascertained via the Family History Assessment Module (Rice et al., 1995) given to the parent(s).

Further screening resulted in the exclusion of individuals with a history of any of the following: schizophrenia, major depressive disorder, bipolar disorder, seizures, major medical disease, regular psychoactive medication use, alcohol or drug dependence (other than nicotine), or uncorrected visual or auditory deficits. Urine and breath samples were collected on the day of testing to exclude subjects who...
had recently used psychoactive substances. Subjects were also asked to abstain from caffeine and nicotine on the day of testing. To eliminate the possible complicating effects of fetal alcohol/drug exposure, subjects whose biological mothers were drinking alcohol or using drugs before or during pregnancy were excluded.

Definition of Subject Groups

For the purpose of analyzing subtypes of conduct problems, subjects were assigned to low (i.e., none) and high severity groups using counts from the Rules Violations, Aggression, Deceitfulness/Theft, and Destructiveness subsets of DSM-IV conduct disorder criteria applied prior to age 15. Because many subjects scored uniformly high, or low, on all of these scales, it was not possible to examine their unique effects using groups that possessed only one subtype. Instead, the analysis of each conduct problem subtype was performed using the same subjects regrouped according to their severity on that subtype. In an attempt to discern the unique effects of each subtype, the statistical effects of the other subtypes were removed by entering them as covariates.

The selection of ≥1 or as the threshold for differentiating low versus high severity groups on all of the subtypes was based on several considerations. These included the different number of criterion items for each subtype, their observed distribution, and power considerations. One might ask whether it is reasonable to expect that subjects reporting 1 conduct problem on any of the scales would differ from subjects reporting 0 conduct problems, because 1 problem could be interpreted as reflecting a “trivial” level of severity. It is important to recognize, however, that each DSM-IV criterion must be so severe as to be expressed behaviorally. Furthermore, many of the criteria for CD are required to be evident on multiple occasions throughout a 6-month period. It would therefore be erroneous to assume that a single truancy from school, or a single episode of “running away” from home, meets our study definition of ≥1 rules violations.

The definition of the age groups was based on the median age of the entire subject sample. The younger group was aged 14–17 years, inclusive. The ages of subjects in the older group ranged between 17 and 20 years, exclusive.

The analytic model applied to the P300 and task performance data for each subtype was a set of severity group (0 versus ≥1) by age group (≤17 years old versus >17 years old) analyses of variance (ANO Vas). Three covariates were entered into each analysis. The covariates were the full range of severity scores for each of the remaining subtypes of conduct problems. An identical set of ANOVAs was performed without covariates. This second set of analyses revealed the identical pattern of group differences described below. They will therefore not be reported.

Task Procedures

The auditory performance task involved the presentation of two pure tones and a white noise burst arranged in random order, with the restriction that white noise bursts were separated by a minimum of 4 pure tone stimuli. The number of pure tone stimuli was restricted to 160. The number of white noise bursts was restricted to 40. The stimuli were 50 msec in duration and presented every 2.5 sec.

At the initiation of the task, the subject was asked to press a button located under his right index finger in response to the higher-pitched (1,000 Hz) tone and a button located under the left index finger in response to the lower-pitched (500 Hz) tone. The subject was told that the correspondence between the correct response button and the tones reverses whenever a white noise burst occurs. Therefore, the response must also reverse. Subjects were required to practice the task to ensure comprehension of task instructions. P300 ERP's elicited by the white noise bursts, which cued the change in stimulus-response mapping, were recorded.

A program was developed and executed for computing the number of trials on which the subject responded to the pure tone trial immediately following a white noise burst, but failed to change his response set (i.e., a perseveration error). The program also counted the number of pure tone stimuli, immediately following a white noise burst, to which the subject correctly responded or failed to respond.

ERP Recording Methods

The subject was seated in a sound-attenuated chamber and wore a fitted electrode cap (Electro-Cap International, Inc.) containing 31 electrodes. A reference electrode was placed on the tip of the nose and a mid-frontal electrode served as the ground. A pair of electrodes was placed diagonally above and below the left eye for detection of eyeblink and eye movement artifacts. Inter-electrode impedances were maintained below 5 KΩ.

The 31 EEG channels and 1 eye movement (EOG) channel were amplified (EEG gain = 20K, EOG gain = 2K) and filtered (bandpass = 0.01–30 Hz) using a Grass Instrument Co. Neurodata Acquisition System. The EEG and EOG channels were routed to an A/D converter (along with markers indicating stimulus and response onsets) and sampled at a rate of 250 Hz for 100 msec preceding and 900 msec following the onset of each cue stimulus. During off-line computations, single trial data were sorted by electrode. Before averaging, trials with eye movement artifacts (i.e., EOG deviation >50 μV) or A/D converter overflow were removed. Time-point averaged waveforms were then created. P300 was identified as the peak voltage in the ERP waveform, between 250 and 700 msec following the onset of the cue stimulus. P300 amplitude was expressed as the difference in microvolts between this peak and the average voltage during the 100-msec prestimulus period. P300 latency was expressed as the time difference between the peak and stimulus onset. To reduce the number of dependent variables and protect against type I error, a principal components analysis (PCA) was performed. The input to the PCA was the correlation matrix of P300 amplitudes measured at 31 electrode sites. Variimax rotation of the principal components yielded two orthogonal factors (eigenvalues >1.0) which collectively explained 83.1% of the total variance. The electrode sites loading highest on the first factor included 18 sites located along or posterior to the central sulcus: T7, C5, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, PO1, PO2, O1, O2. The second factor included 13 electrode sites principally located over the frontal lobes: FP1, FP2, AF1, AF2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6. P300 amplitude and P300 latency were averaged across the electrodes within each factor, generating mean values for each of the two regions.

P300 Topographic Analyses

The topographic localization of P300 utilized a three-compartment model computed using the BEM. This method has been shown to be superior to the three-shell spherical model because it is constrained by realistic head shape geometry and by the thickness of each compartment. Indeed, when the current source resides in either frontal or temporal brain regions, the BEM model is highly preferred (Fuchs et al., 1998).

Ideally, a separate BEM calculation should occur for each subject so as to minimize interindividual variation in the thickness of the compartments. However, it was not possible to obtain magnetic resonance imaging scans (MRIs) from the entire sample of 94 study subjects. Rather, group-averaged data were fitted to a single MRI obtained from a single, 17-year-old male. The following compartment parameters were used to constrain the BEM model: 3 mm skin thickness, 9 mm skull thickness,
and 2 mm cortical thickness. The transformation of electrode locations and MRI data into the same coordinate system was accomplished using the CURRY software package (Neuroscan, Inc., Herndon, VA).

Localization of the P300 difference, between 250 and 700 msec post-stimulus onset, occurred by converting scalp potential data to CSD estimates (Hjorth, 1980). The calculation of a CSD map is roughly equivalent to the application of a high-pass spatial filter that, when applied to common-referenced data, markedly reduces the electrical distortions produced by the skull and scalp. For the present analysis, CSD measurements were obtained for each of 3,394 triangles that estimated the cortical surface. These measurements were converted to z scores for analysis. Z statistics that exceeded a value of 3 standard deviation units ($p < .005$) were deemed significant.

**RESULTS**

**Background Characteristics**

The first stage in the analysis was an examination of the background demographic, alcohol use, and family history characteristics of the study groups. Tests of group equivalence on continuous measures were performed using 2 (severity) by 2 (age) ANOVAs. Group equivalence on categorical measures was determined by Pearson $\chi^2$ tests. The results of these analyses are presented in Table 1.

As can be seen in Table 1, the prevalence of paternal alcohol, cocaine, and heroin dependence was approximately 50% in all of the groups, resulting from the recruitment strategy. The percentage of subjects with either the combined, inattentive, or hyperactive-impulsive subtypes of attention-deficit/hyperactivity disorder (ADHD) was uniformly low (i.e., 1.4%, 6.9%, and 0%, respectively). The groups did not differ significantly on either of these variables.

Significant main effects of age group were found on educational attainment in the analyses of all four conduct

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Background Characteristics: Mean (SD) or Percent</th>
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<tbody>
<tr>
<td>Rules Vio = 0</td>
<td>Rules Vio = 0</td>
</tr>
<tr>
<td>Age Group ≤ 17</td>
<td>Age Group &gt; 17</td>
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<tr>
<td>n</td>
<td>12</td>
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<tr>
<td>% White $^a$</td>
<td>66.7</td>
</tr>
<tr>
<td>Years of education $^{a,b}$</td>
<td>8.8 (0.8)</td>
</tr>
<tr>
<td>MAST score $^c$</td>
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</tr>
<tr>
<td>% FH of substance dependence</td>
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<tr>
<td>Aggress = 0</td>
<td>Aggress = 0</td>
</tr>
<tr>
<td>Age Group ≤ 17</td>
<td>Age Group &gt; 17</td>
</tr>
<tr>
<td>n</td>
<td>31</td>
</tr>
<tr>
<td>% White $^a$</td>
<td>64.5</td>
</tr>
<tr>
<td>Years of education $^{a,b}$</td>
<td>8.8 (0.8)</td>
</tr>
<tr>
<td>MAST score</td>
<td>2.6 (4.1)</td>
</tr>
<tr>
<td>% FH of substance dependence</td>
<td>64.5</td>
</tr>
<tr>
<td>Deceit = 0</td>
<td>Deceit = 0</td>
</tr>
<tr>
<td>Age Group ≤ 17</td>
<td>Age Group &gt; 17</td>
</tr>
<tr>
<td>n</td>
<td>25</td>
</tr>
<tr>
<td>% White</td>
<td>52.0</td>
</tr>
<tr>
<td>Years of education $^d$</td>
<td>8.8 (0.9)</td>
</tr>
<tr>
<td>MAST score</td>
<td>1.6 (2.7)</td>
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<tr>
<td>% FH of substance dependence</td>
<td>64.0</td>
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<tr>
<td>Destruct = 0</td>
<td>Destruct = 0</td>
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<tr>
<td>Age Group ≤ 17</td>
<td>Age Group &gt; 17</td>
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<td>n</td>
<td>22</td>
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<tr>
<td>% White</td>
<td>40.9</td>
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<tr>
<td>Years of education $^d$</td>
<td>8.8 (0.8)</td>
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<tr>
<td>MAST score $^e$</td>
<td>2.5 (3.7)</td>
</tr>
<tr>
<td>% FH of substance dependence</td>
<td>63.6</td>
</tr>
</tbody>
</table>

Note: MAST = Michigan Alcoholism Screening Test; FH = family history.

$^a$ Age group main effect, $p < .05$.

$^b$ Severity main effect, $p < .05$.

$^a,b$ Age group $\times$ severity interaction, $p < .05$. 
problem subtypes: Rules Violations, \( F_{1,90} = 73.8, p < .001 \); Aggression, \( F_{1,90} = 69.1, p < .001 \); Deceitfulness/Theft, \( F_{1,90} = 63.8, p < .001 \); Destructiveness, \( F_{1,90} = 80.5, p < .001 \). An examination of the means reveals an obvious result: older adolescents had successfully completed more years of education than younger adolescents. In the analysis of the Rules Violations (\( F_{1,90} = 3.4, p < .05 \)) subtype, a significant interaction between severity and age group was found. Tukey post hoc tests revealed that older subjects with conduct problems of the Rules Violations type attained a lower grade level than older subjects without rules violations. Among younger subjects, the absence versus presence of rules violations was not associated with a difference in educational attainment.

Analyses of the number of alcohol use–related problems from the Michigan Alcoholism Screening Test (Selzer, 1971) revealed a significant main effect of severity for the Rules Violations (\( F_{1,90} = 8.8, p < .005 \)) and Destructiveness (\( F_{1,90} = 8.0, p < .05 \)) subtypes. Subjects reporting rules violations and destructive behaviors reported more alcohol use–related problems than subjects who did not exhibit these behaviors.

### Task Performance

On average, subjects responded correctly on 55% of the trials immediately following the cue stimulus. They failed to switch response sets on 38.9% of the trials. The percentage of trials with omission errors averaged 21.5%. Task performance measures obtained from each group are presented in Table 2.

Older subjects exhibited significantly fewer perseveration errors than younger subjects regardless of the type and severity of their conduct problems: Rules Violations, \( F_{1,87} = 4.4, p < .05 \); Aggression, \( F_{1,87} = 6.6, p < .05 \); Deceitfulness/Theft, \( F_{1,87} = 4.9, p < .05 \); Destructiveness, \( F_{1,87} = 6.1, p < .05 \). In addition to this main effect of age, a main effect of severity was found for the Aggression subtype only: \( F_{1,87} = 10.4, p < .001 \). Aggressive adolescents exhibited more perseveration errors than nonaggressive adolescents.

Aging was associated with an increased number of correct responses in the analyses of the Rules Violations (\( F_{1,87} = 3.8, p < .05 \)), Aggression (\( F_{1,87} = 5.2, p < .02 \)), Deceitfulness/Theft (\( F_{1,87} = 5.3, p < .02 \)), and Destructiveness

<p>| TABLE 2 |</p>
<table>
<thead>
<tr>
<th>Task Performance: Covariate-Adjusted Mean (SD)</th>
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<tbody>
<tr>
<td>Rules Vio = 0</td>
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<tr>
<td>Age Group ≤ 17</td>
</tr>
<tr>
<td>Perseveration errors (^a)</td>
</tr>
<tr>
<td>No. correct (^a)</td>
</tr>
<tr>
<td>No. omissions</td>
</tr>
<tr>
<td>Age Group main effect, ( p &lt; .05 ).</td>
</tr>
<tr>
<td>Rules Vio = 0</td>
</tr>
<tr>
<td>Age Group ≤ 17</td>
</tr>
<tr>
<td>Perseveration errors (^a,b)</td>
</tr>
<tr>
<td>No. correct (^a)</td>
</tr>
<tr>
<td>No. omissions</td>
</tr>
<tr>
<td>Deceitfulness main effect, ( p &lt; .05 ).</td>
</tr>
<tr>
<td>Rules Vio = 0</td>
</tr>
<tr>
<td>Age Group ≤ 17</td>
</tr>
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<td>Perseveration errors (^a)</td>
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<td>No. correct (^a,b)</td>
</tr>
<tr>
<td>No. omissions</td>
</tr>
<tr>
<td>Destructiveness main effect, ( p &lt; .05 ).</td>
</tr>
</tbody>
</table>

\(^a\) Age group main effect, \( p < .05 \).  
\(^b\) Severity main effect, \( p < .05 \).  
\(^a,b\) Age group \( \times \) severity interaction, \( p < .05 \).
(F_{1,87} = 6.2, p < .02) subtypes. Age group and severity interactively affected the number of correct responses only for the Deceitfulness/Theft subtype (F_{1,87} = 7.2, p < .009). Tukey post hoc tests showed that aging was associated with improved performance among subjects lacking Deceitfulness/Theft problem behaviors. Yet aging did not improve the correct response rate of subjects who exhibited these behaviors.

P300 Amplitude

Separate analyses of frontal and posterior region P300 amplitude were conducted across the four conduct problem subtypes. The results of these analyses are illustrated in Figure 1. Representative waveforms, averaged by the severity of the Rules Violations subtype, and derived from 3 (Fz, Cz, Pz) of the 31 electrode sites are presented in Figure 2.

Age group and severity interactively affected P300 among subjects organized by the Rules Violations subtype. The interaction of severity and age group was significant within both frontal (F_{1,87} = 7.0, p < .01) and posterior (F_{1,87} = 5.9, p < .02) regions. Tukey post hoc tests revealed that frontal and posterior region P300 amplitude both increased with age among boys who lacked conduct problems of the Rules Violations type. Among boys with rules violations, however, frontal and posterior region P300 amplitude did not change with age.

A significant main effect of age group was also found in the analysis of the Rules Violations subtype. This effect was only significant within the frontal region (F_{1,87} = 4.3, p < .05). It did not attain significance within the posterior region (F_{1,87} = 2.3, p = .13). The effect of age was to increase frontal P300 amplitude by an average of 2.7 µV.

As Figure 1 shows, none of the other conduct problem subtypes significantly altered P300 amplitude.

P300 Latency

Analyses of covariance (ANCOVAs) of frontal and posterior region P300 latency revealed no significant changes as a function of age group or the type and severity of conduct problems.

P300 Topography

The source reconstruction method was applied to the difference waveform obtained by subtracting the group-averaged ERP for younger subjects from the ERP averaged for older subjects. Because the Rules Violations subtype was shown in the prior analyses to contribute systematic variance to P300, the topographic analysis of the effects of age was conducted only for the two severity levels of this subtype. No other subtypes were analyzed topographically. The results of the CSD/BEM calculation are illustrated in Figure 3.

Areas within Figure 3 rendered in either yellow or green represent areas that significantly differentiated among the two age groups. As can be seen in the left half of the figure, aging among adolescents without rules violation problem behaviors was associated with increased activation in some posterior brain regions, in the vicinity of the angular gyrus, and in some frontal brain regions, in
the vicinity of the left superior and middle frontal gyri. CSD/BEM topographic maps for adolescents with rules violation problem behaviors revealed a topographically different pattern of P300 maturation (see right side of Fig. 3). Within the posterior brain, the effect of aging was equivalent to that seen in subjects without rules violations. In contrast, the effect of aging within the frontal brain was not significant (see arrow).

**DISCUSSION**

One goal of this study was to determine whether the relationship reported previously (Bauer and Hesselbrock, 1999a) between P300, conduct problems, and brain maturation would generalize to an auditory task that placed high demands on response regulation. This goal was met. Adolescents with conduct problems exhibited a dampened, and almost absent, change in P300 amplitude as a function of age.

The second goal—that is, to demonstrate neurophysiological differences among the subtypes of CD—was
also met. In one previous study (Bauer and Hesselbrock, 1999b) of adolescents performing the Stroop Test, subtypes of conduct problems were examined and Rules Violations was also found to be the only subtype associated with a P300 amplitude reduction. The absence of significant effects of other conduct problem subtypes on P300 in both the present and previous studies may be an artifact of our decision to recruit subjects from the community rather than juvenile justice or substance abuse treatment programs. As a result of this sampling strategy, the prevalence and severity of aggressive, deceitful, and destructive behaviors may have been muted.

There are other explanations for the selective and more pronounced effects of the Rules Violations subtype. For example, it is important to note that each DSM-IV criterion for rules violations behaviors must be met on multiple occasions before the criterion can be counted toward the diagnosis. In contrast, the DSM-IV criterion items comprising the other subtypes of conduct problems can be counted toward a diagnosis if they occur only once. Thus, a count of ≥1 diagnostic criteria from the Rules Violations category implies a higher level of severity and/or frequency of conduct-disordered behavior.

Another potential explanation for the pronounced association between rules violations and brain function (i.e., P300) involves the nature of rules violation behaviors. Repeated episodes of truancy from school, “running away” from home, and defiance of rules in the face of prohibitions are conduct problems that are usually deliberated upon prior to execution. Furthermore, and unlike most other types of conduct problems, no outside persons or precipitants are needed for these behaviors to be expressed or reinforced. One might conceptualize rules violation–type behaviors as reflecting a planned and consistent pattern of dysfunctional behavior rather than an impulsive and inappropriate reaction to an environmental precipitant. Accordingly, rules violations might be associated with a more pronounced alteration in brain function than the other subtypes.

A third alternative explanation involves the lower degree of overlap of the Rules Violations subtype with the other subtypes. In fact, a cross-tabulation of the number of subjects with unique or overlapping subtypes of conduct problems revealed that 11 subjects had no problems of any type and 14 subjects had conduct problems only of the Rules Violations subtype. But the vast majority of subjects exhibited conduct problems of multiple types. Therefore, the effects of the Aggression, Deceitfulness/Theft, and Destructiveness subtypes on P300, and their inter-

actions with brain maturation (Fig. 1), are more contaminated by the effects of overlap than are the effects of the Rules Violations subtype. We attempted to control for the overlap via ANCOVA. However, one must recognize that ANCOVA has its limitations. We have also conducted additional analyses (available on request) comparing the 11 subjects with no conduct problems of any type to the four conduct problem subtypes. The results of those analyses were identical with those reported here.

The absence of a significant effect of the Rules Violations subtype on task performance, and most particularly upon the number of perseveration errors, is somewhat perplexing. One must recognize, however, that the stimulus that evoked the P300 for this study was a cue, and was not the stimulus to which subjects were asked to respond. Accordingly, the cognitive processes reflected in the P300 were most likely related to orienting or alerting, whereas behavioral performance was more directly related to response reversal or perseveration. In this context, it is less surprising that the Rules Violations subtype had a greater effect on P300 and the Aggression subtype had a greater effect on the number of perseveration errors. From their differing effects on task performance and P300, one could hypothesize that these subtypes are behaviorally and neurophysiologically different.

The neuroanatomical location of the main effect of age is intriguing. Within the analysis of the Rules Violations subtype, a significant main effect of age was found for the frontal region only (Fig. 1, top left). In fact, numerous studies using either autopsy material (Huttenlocher, 1979; Huttenlocher et al., 1987) or structural MRI techniques (Jernigan et al., 1991; Pfefferbaum et al., 1994) have shown that frontal brain regions undergo pronounced morphological changes throughout adolescence. Other brain regions attain morphological stability by age 12. The present finding of an increase in frontal P300 amplitude, between 14 and 19 years of age, is consistent with these autopsy and MRI findings.

Frontal brain regions were also particularly sensitive to the interaction between the Rules Violations subtype and aging. The CSD maps presented in Figure 3 show that adolescents with this subtype (lower right panel) fail to show the same maturational increase in frontal P300 CSD found in adolescents without rules violation behaviors (lower left panel). In contrast, P300 CSDs measured in posterior brain regions increased equally with age in the Rules Violations = 0 and Rules Violations ≥ 1 groups. In the broader context, these results are consistent with
evolving theories of ADHD and other disruptive behavior disorders. Patients with ADHD have been documented as exhibiting smaller changes in brain structure (Durston et al., 2001; Rapoport et al., 2001) and function (Johnstone et al., 2001) during adolescence.

In summary, the results of this study lend further credence (Bauer and Hesselbrock, 1999a; Hill et al., 1999; Mezzacappa et al., 1999; Tarter et al., 1999) to the hypothesis that heightened risk for adult psychopathology is associated with impaired brain maturation. The results also show that conduct problems—the risk factor studied herein—is not a homogenous entity. The presence of conduct problems in the Rules Violations category was most strongly associated with impaired brain maturation. CSD calculations constrained by a boundary element model showed that the maturation of frontal brain regions, in the vicinity of the left superior frontal gyrus, is different among adolescents with a history of rules violation behaviors. Numerous P300 studies (Bauer, 1997; Bauer et al., 1994a,b; Costa et al., 2000; O’Connor et al., 1994) of adults with ASPD suggest that this deficit in frontal brain function does not resolve in adulthood.

Limitations

In this study, the P300 ERP was a valuable metric for revealing subtle neurophysiological abnormalities that underlie conduct problems. It is important to acknowledge, however, that P300 abnormalities are not specific to this childhood disorder. Similar neurophysiological changes have been documented in association with a wide variety of psychiatric and neurological problems. It is also true that P300 abnormalities have been described among the relatives of patients with schizophrenia, major depressive disorder, and alcoholism. The P300 abnormality found in this study among otherwise healthy adolescent males should therefore only be viewed as a nonspecific marker of increased risk for a variety of potentially unfortunate outcomes.

A second limitation relates to CSD modeling. CSD can only provide an approximate localization of the current source. It is not ideal for revealing activation of, or group differences in, subcortical sources. The number and density of the electrode montage also constrain its spatial resolution.

Clinical Implications

The present findings are preliminary and have no significant clinical implications at this time. Because female adolescents generally exhibit fewer CD problems than their male counterparts, and this study was limited to males, the aforementioned findings might not derive from a study of a general clinic population. It would nonetheless be interesting to conduct such a study and evaluate whether altered brain maturation is predictive of clinically significant problems in adulthood.

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