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Neurosteroid blood levels in delinquent adolescent boys with conduct disorder

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Abstract

Accumulating data indicates that neurosteroids can modulate aggressive behavior. The aim of the present study was to examine neurosteroid blood levels in delinquent adolescent boys as compared to normal healthy controls. Dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S) and cortisol blood levels were measured in 16 delinquent adolescent (age 15.72 ± 0.95 years) with conduct disorder (CD) and 11 normal controls (16.82 ± 1.83 years). Severity of aggressive behavior was assessed by the Child Behavior Checklist (CBCL) and the Overt Aggression Scale (OAS). The delinquent adolescents tended to have higher DHEA-S levels than the normal control group ($p = 0.054$). DHEA and cortisol levels did not differ between the two groups. The interaction between neurosteroids (especial DHEA-S) and genetic, developmental and environmental factors in juvenile delinquency merits further investigation.

1. Introduction

There is growing evidence of the involvement of neurosteroids in adolescents' aggression and violence (for review see Golubchik et al., 2007). Their modulatory effect on aggressive behavior may be related to their activity at the gamma-aminobutyric acid (GABA)-A receptor (Miczek et al., 2003). Several studies evaluated adrenal axis homeostasis and neurosteroid levels in adolescent aggressive populations, but the results are still inconsistent and the conclusions are ambiguous. Constantino et al. (1993) assessed circulatory DHEA and DHEA-S in 18 aggressive prepubertal boys, hospitalized for violent behavior at a children's psychiatric facility and diagnosed with conduct disorder (CD). They did not find significant differences between aggressive and non-aggressive children in the levels of both neurosteroids. Later, Van Goozen et al. (1998) examined the relationship between androgens and aggression in prepubertal boys who exhibited severe

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aggressive behavior. Blood DHEA-S levels were measured in 15 CD boys and 25 normal control boys. The CD boys had significantly higher levels of DHEA-S than the controls, and DHEA-S levels were significantly positively correlated with the intensity of aggression and delinquency, as rated by both parents and teachers. The same group (Van Goozen et al., 2000) examined the relationship between DHEA-S levels and aggression in children with oppositional defiant disorder (ODD) and compared their levels with a control group with other psychiatric conditions [about half of then with attention-deficit hyperactivity disorder (ADHD)] as well as with normal controls. Children with ODD had higher DHEA-S levels compared to both the psychiatric control group and the healthy one. Interestingly, it was possible to classify children as having either ODD or ADHD on the basis of their DHEA-S levels. Also noteworthy, Strous et al., (2001) found in ADHD children an inverse correlation between circulatory DHEA levels and ADHD severity. Moreover, beneficial effect of methylphenidate treatment in ADHD patients was associated with an increase in circulatory DHEA and DHEA-S levels (Maayan et al., 2003; Lee et al., in press). Dimitrieva et al. (2001) reported an association of aggression and dysregulation of the adrenal axis. They evaluated 28 CD children and 13 controls (10–18 years old) for levels of DHEA-S. Higher DHEA-S levels were found in the CD children. They also found a positive correlation between DHEA-S levels and disruptive behavior. Another study (Buydens-Branchey and Branchey, 2004) found that adult cocaine addicts with a retrospective diagnosis of CD had significantly increased DHEA-S levels and a decreased cortisol reactivity to stressful situation. The results indicated that mechanisms underlying neurosteroid and cortisol alterations in childhood may play a role in adulthood as well.

The aim of the present study was to examine neurosteroid blood levels in delinquent CD adolescent boys, including different parameters of aggression, as compared to normal healthy controls.

2. Methods

2.1. Subjects

The study included sixteen delinquent adolescents and 11 normal control adolescents aged 14–19 years. At the time of the clinical referral all the delinquent adolescents met DSM-IV-TR diagnostic criteria for conduct disorder (CD) (APA, DSM-IV-TR, 2000). They were violent subjects referred by the Adolescent Correctional Services of the Ministry of Social Welfare and were admitted consecutively.

2.2. Diagnosis and scales

The diagnosis of CD was established according to the DSM-IV-TR criteria. The comparison group consisted of 11 healthy volunteers without physical or psychiatric disorders from the same region. In order to establish the psychiatric diagnoses a consensus was required between two board certified senior child and adolescent psychiatrists (PG and TM). The severity of CD was assessed by the child behavior checklist, aggression subscale, teacher form (CBCL; Achenbach et al., 1991). In addition, the level of aggression of the CD subjects was evaluated by the Overt Aggression Scale (OAS; Yudofsky et al., 1986) was completed by the mental health social worker of the Adolescent Correctional Services.

Additional data regarding the age of entry to a correctional facility and history of violence or sexual violence was collected from the subjects' records. The delinquent CD adolescents were divided into groups, according to their criminal records. One group of sexually aggressive boys ($n=6$) and another of boys without sexual assault records ($n=9$) and also a group of CD adolescents with records of violent crimes ($n=9$) and another without such assault records ($n=7$).

All participants were medication-free for at least 2 months prior to the study. Adolescents with a history of psychosis and current substance abuse were excluded from the study. The study was approved by the Geha Mental Health Center's Institutional Review Board and by the Ministry of Health's Board for Human Clinical Studies. All participants and their parents gave written informed consent for participation in the study.

2.3. Laboratory methods

Blood samples from all CD adolescents and all controls were collected in the morning (at 9:00 a.m–11:00 a.m).

DHEA was measured with the DHEA-DSL 9000 Active™ DHEA coated tube radioimmunoassay (RIA) kit (Diagnostic System Laboratories, Webster, TX, USA); sensitivity 0.2 ng/ml; cross reactivity with DHEA-S 0.88%.

DHEA-S was assessed with the DHEA-S-DSL-3500 Active™ DHEA-S coated tube RIA kit (Diagnostic System Laboratory, Webster, TX. USA); sensitivity 4.6 ng/ml.

Cortisol was measured by the TKCO1 Coat-A-Count kit (Diagnostic Products Corporation, Los Angeles, CA, USA); sensitivity 0.2 μg/dl. The intra-assay variability values for cortisol, DHEA, and DHEA-S are 3–4.8%, 5.6–10.6%, and 6.3–9.4%, respectively.

The samples of the patients and controls were run in the same assay to avoid inter-assay variances.

2.4. Statistical analysis

Differences between the CD and control participants as well as differences between the subgroups were analyzed with unpaired t test, including Welch's correction as appropriate. Correlations between the steroids and psychometric variables were analyzed with Pearson's correlation coefficient test. A Bonferroni's correction for multiple comparisons was applied as appropriate. All results are expressed as mean ± SD.

2.5. Results

The mean age of the CD delinquent adolescents ($n=16$; 15.72 ± 0.95 years) did not differ significantly from the control group ($n=11$; 16.82 ± 1.83 years) : $t=1.99$, $df=24$, $p=0.06$. The majority of patients were admitted to the correctional facility in their mid-adolescence (mean age of entry to the institution was 15.18 ± 0.82 years).

The CD delinquent patient and control groups did not differ significantly in the circulatory levels of either DHEA [delinquent adolescent group ($n=16$) 35.25 ± 17.76 nmol/l vs. control group ($n=11$) 33.36 ± 19.18 nmol/l, $t=0.2626$; $df=25$, $p=0.80$] or cortisol [delinquent adolescent group ($n=16$) 389 ± 165 vs. control group ($n=11$) 486 ± 130 nmol/l, $t=1.63$; $df=25$, $p=0.12$]. A tendency towards higher DHEA-S levels (+65%) was