The impact of pre-and perinatal factors on attention-deficit and disruptive behavior disorders

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SUMMARY: Şenol S, Şener Ş, Ergenekon E, Gücüyener K. The impact of pre- and perinatal factors on attention-deficit and disruptive behavior disorders. Turk J Pediatr 2001; 43: 231-236.

Diagnosis of attention-deficit and disruptive behavior disorders defines a group of disorders which have common properties. This group consists of attention-deficit hyperactivity disorder, conduct disorder and oppositional defiant disorder. In order to differentiate these disorders, which share similar properties, it is important to verify the existing differences. In this respect, differences between and distribution of perinatal factors in these three disorders were investigated. The study was conducted in the Child Psychiatry and Pediatric Neurology Departments over a 20-month period. Two hundred and seventy children out of 1,556 attendant with various complaints were diagnosed to have one of the following disorders: 121 had attention-deficit hyperactivity disorder, 50 had oppositional defiant disorder and 99 had conduct disorder. The prenatal and perinatal data of the patients were evaluated retrospectively by a neonatologist. With regard to the investigated parameters, none showed any significant difference between the three groups when compared. The three disorders, which share many similarities in terms of the symptoms, also show similarities in terms of perinatal factors. Since we did not find any study similar in design, our results, although statistically not significant, are discussed in light of the little data available.

Key words: attention-deficit and disruptive behavior disorders, perinatal risk factor.

"Attention-deficit and disruptive behavior disorders (ADDBD)" diagnosis is used to define a group of disorders which start during childhood and adolescence and share common clinical features. It is thought that three different but closely related behavioral patterns lie beneath the basis of these disorders. These are attention-deficit/learning-deficit, hyperactivity/impulsivity and problem behavior[1]. The World Health Organization's[2] International Classification of Mental and Behavioral Disorders: Diagnostic Criteria (ICD-10) for Research includes hyperkinetic and conduct disorders under "behavioral and emotional disorders occurring in childhood and adolescence". The same disorders are under the general heading of ADDBD in the American Psychiatric Association's[3], The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). This group includes attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD) and oppositional defiant disorder (ODD). These three disorders are also defined as externalizing disorders[4].

Attention-deficit/hyperactivity disorder, a heterogeneous disorder, is a major clinical and public health problem throughout the world. DSM-IV[3] recognizes three subtypes of ADHD: predominantly inattentive predominantly hyperactive impulse, and combined. The diagnosis is established on the basis of history of symptoms representing the cardinal constructs of ADHD: inattention, impulsiveness and hyperactivity. Low birth weight was identified by the National Collaborative Perinatal Project (NCPP)[5] as a clear risk factor for ADHD. Klebans et al.[6] made comparisons among the four birth weight groups: extremely low birth weight (ELBW), very low birth weight (VLBW), low birth weight (LBW) and normal birth weight (NBW). The ELBW children had lower attention and lower overall social competence than all other birth weight groups as measured by classroom teachers[6]. All LBW children had lower attention and higher day dreaming and hyperactivity scores than NBW children.

Research on premature infants provides some clues to the neuroanatomy of ADHD. Dynamic imaging studies of children have shown that ADHD is associated with lowered glucose metabolism primarily in the periventricular areas and the prefrontal cortex[7]. In the susceptible prematures, germinal matrix-intraventricular hemorrhage-related lesions in the caudate nucleus may disrupt the migration of cells from the germinal matrix to subcortical structures such as the thalamus and then to the prefrontal cortex[8,9].

Another longitudinal group of studies showed that germinal matrix hemorrhage has been associated with more subtle cognitive difficulties in attention, spatial memory and ability to inhibit behaviors (frontal cortex functions)[10,11].

Although this disorder has been recognized in children prior to age three, it may be difficult to distinguish preschool children with ADHD from those with conduct or oppositional defiant disorders. Most children can be diagnosed by age six to seven by entering primary school, when their externalizing symptoms are most evident. Due to the diagnostic difficulties, there is a wide array of prevalence rates reported, ranging between 2-5%[3,12-15].

Lately an improved understanding of the neurobiology along with genetics of ADHD, and of diseased areas in the brain has been achieved, stressing the importance of the striatum and corticostriato-thalamocortical loops as a substrate for the disorder[16]. Among the lesional factors, pre-and perinatal events are the leading ones[17]. Recent studies have also implicated prenatal and perinatal events[18,19], prematurity, the medical status of the mother before and during pregnancy[20,21], and complicated pregnancy/labor as risk factors for ADHD[22]. Öktem and Sonuvar[23] presented the demographic variables of children diagnosed as ADHD including birth, early development, family characteristics, and mental and neurological signs during a ten-year period.

In this respect the purpose of the present study was to investigate whether pre-and perinatal events have any special effect as a risk factor on disruptive behavioral disorders (conduct disorder or oppositional defiant disorder) when compared to ADHD.

Material and Methods

The study included 270 children who had ADDBD, out of 1,556 who were referred to Gazi University Faculty of Medicine Departments of Child Psychiatry and Pediatric Neurology due to various illnesses over a period of 20 months. All referred children were independently evaluated by two child psychiatrists according to DSM-IV criteria[3], during an interview. All children diagnosed to have ADDBD by both child psychiatrists were included in the study and subtyped further according to DSM-IV criteria (Table I). During the interview every DSM-IV criterion for the relevant disorder was scored by the evaluating psychiatrist, giving a maximum total score of 9 for predominantly inattentive type ADHD, 9 for predominantly hyperactive impulsive type ADHD, 8 for ODD and 15 for CD. These scores were used in the comparisons.

Table I. Diagnosis of the Patients According to DSM-IV Criteria

DSM-IV diagnosis	n	%
Attention-deficit and disruptive behavior disorders	270	17.4
Attention-deficit/hyperactivity disorder	121	7.8
Oppositional defiant disorder	50	3.2
Conduct disorder	99	6.4
Other DSM-IV dignoses	1166	74.9
No diagnosis (developmental complaint)	120	7.7
Total	1556	100.0

All the children were required to have an IQ above 70, to be medically healthy and nonpsychotic, and to have no abnormality according to their neurological examination made by a pediatric neurologist. The medical records of the mothers and children were evaluated by a neonatologist, the pre-perinatal period, early postnatal events and post medical history. Any psychiatric disorders alone or associated with ADDBD were also screened.

All the children were evaluated by classroom teachers who observed the children with regard to the 28 questions comprising the Conners' Teacher Rating Scale[24-27]. The adaptation of the rating scale to Turkish children was made by Şener et al.[28] Conners' Parent Rating Scale consisted of 48 questions, and Turkish adaptation was made by Dereboy et al.[29].

Statistical analysis was performed by SPSS for Window (Statistical Package for Social Sciences for Windows. Release 6.0 SPSS Inc. (1989-1993). Student's test was used to compare differences between the groups, with $p < 0.05$ accepted as significant and all others as non-significant.

Results

During the 20-month period, of the 1,556 children referred, 270 patients were evaluated. The mean age of the 270 patients (202 male, 74.8%; 68 female, 25.2%) included in the study was 10.6 ± 3.3 (range 6-16 years) and the diagnoses are shown in Table I.

Some of the subjects in the ADDBD group were found to also have other co-morbid disorders of the same group. While 83 subjects in the ADHD group did not have any other co-morbid disorder of the same diagnosis group, 38 were diagnosed to have CD of ODD, in addition to ADHD (Table II). The clinicians were asked to establish the primary diagnosis for every case for statistical analysis. Further comparisons were performed according to those diagnoses.

Table II. Comorbid Diagnosis of Patients in the ADDBD Group and Association with Hypoxia

DSM-IV diagnosis	n	%	Hypoxia +
ADHD-IA	13	4.9	1
ADHD-HA	16	5.9	–
ADHD-C	54	20.0	5
ODD	23	8.5	3
CD	93	34.5	2
ADHD-IA+ODD	3	1.1	1
ADHD-HA+ODD	9	3.3	–
ADHD-IA+CD	6	2.2	–
ADHD-HA+CD	12	4.4	–
ADHD-C+ODD	17	6.3	1
ADHD-C+CD	24	8.9	2
Total	270	100.0	15

ADHD-IA: Attention-deficit hyperactivity disorder, predominantly inattentive type. ADHD-HA: Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type. ADHD-C: Attention-deficit hyperactivity disorder, combined type. ODD: Oppositional defiant disorder. CD: Conduct disorder. ADDBD: Attention-deficit and disruptive behavior disorders.

Statistical comparison between hypoxic and non-hypoxic subjects according to secondary diagnoses was not done, as the sample sizes were quite small in most groups. However eight out of 10 subjects in the hypoxic group had a secondary diagnosis, while only 50 of the 111 subjects in the non-hypoxic group had secondary diagnoses; the difference was statistically significant ($\chi^2 = 7.63$, $p < 0.01$) (Table III).

All 270 patients diagnosed to have ADDBD were grouped according to the following criteria: unexpected or a planned pregnancy, gestational age, type of pregnancy, birth complications (icnluding hypoxia) and birth weight (Table IV).

About one fourth of the patients were born after an unplanned pregnancy; nearly all of the ADDBD patients had a history of planned pregnancy.

Except for planned and unexpected pregnancies, where a significant difference between the groups existed ($p < 0.01$), there were not any statistically significant differences between the compared groups with regard to the defined criteria ($p > 0.05$).

The Conners' Teacher and Parent Rating Scales were also compared with reference to birth complications and type of delivery. These data and statistical results are shown in Table V.

With regard to the diagnostic groups of ADDBD, comparison of the scores showed no statistical significance. There was no statistically significant relation among the diagnosis groups (with or without hypoxia) with respect to ADDBD, ADHD, and Conners' Teacher and Parent Rating scores ($p > 0.05$) (Table VI).

Table III. Comorbid Secondary Diagnoses of the 121 Subjects With or Without Coexistence of Hypoxia

	ADHD-IA		ADHD-HA		ADHD-C		Total*	
Comorbid diagnoses	Hypoxia –	Hypoxia +	Hypoxia –	Hypoxia +	Hypoxia –	Hypoxia +	Hypoxia –	Hypoxia +
Depression	2	–	–	–	6	–	8	–
Anxiety disorders	–	–	1	–		–	1	–
Tic disorders	–	–	3	–	4	1	7	1
Enuresis	2	1	4	1	14	2	20	4
Encopresis	–	–	2		3	1	5	1
Stuttering	1	–	–	–	1	–	2	
Learning disabilities	1	1	–	–	3	1	4	2
Other (dyslexia, eating disorders, alopecia areata)	–	–	–	–	3	–	3	–
Total secondary diagnoses	6	2	10	1	34	5	50	8
No secondary diagnoses	8	–	15	–	38	2	61	2
Total*	14	2	25	1	72	7	111	10

ADHD-IA: Attention-deficit hyperactivity disorder, predominantly inattentive type. ADHD-HA: Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type. ADHD-C: Attention-deficit hyperactivity disorder, combined type.
*$\chi^2 = 7.63$, df = 1, $p < 0.01$.

Table IV. Comparison Among the Groups Based on Defined Criteria

	DSM-IV diagnosis											
	ADHD-IA		ADHD-HA		ADHD-C		ODD		CD		Total	
Pregnancy*	n	%	n	%	n	%	n	%	n	%	n	%
Planned	16	100.0	24	92.3	62	78.5	40	80.0	67	67.7	209	77.4
Unplanned	–	–	2	7.7	17	21.5	10	20.0	32	32.3	61	22.6
Duration of pregnancyə												
Preterm	–	1	3.8	11	13.9	7	14.0	6	6.1	25	9.3	
Term	15	93.8	24	92.4	65	82.3	40	80.0	89	89.9	233	86.3
Postterm	1	6.2	1	3.8	3	3.8	3	6.0	4	4.0	12	4.4
Type of laborə												
Spontaneous	13	81.3	22	84.6	59	74.7	42	84.0	81	81.8	217	80.4
C/S	3	18.7	4	15.4	18	22.8	7	14.0	12	12.1	44	16.3
Intervention	–	–	–	–	2	2.5	1	2.0	6	6.1	9	3.3
Hypoxiaə												
no	14	87.5	25	96.2	72	91.1	47	94.0	97	98.0	255	94.4
yes	2	12.5	1	3.8	7	8.9	3	6.0	2	2.0	15	5.6
Birth weightə (g)	ADHD-IA A.mean±Sd		ADHD-HA A.mean±Sd		ADHD-C A.mean±Sd		ODD A.mean±Sd		CD A.mean±Sd		F	significant
	3228.13 ± 407.0		3353.08 ± 503.7		3423.04 ± 583.7		3295.00 ± 583.0		3413.74 ± 519.0		0.850	> 0.05

A.mean ± Sd: arithmetic mean ± standard deviation.
ADHD-IA : Attention-deficit hyperactivity disorder, predominantly inattentive type.
ADHD-HA : Attention-deficit hyperactivity disorder, predominantly hyperactive impulsive type.
ADHD-C : Attention-deficit hyperactivity disorder, combined type.
ODD : Oppositional defiant disorder.
CD : Conduct disorder.
C/S : Cesarean section.
* $\chi^2 = 13.57$, df = 4, $p < 0.01$.
ə not statistically significant.

Table V. Conners' Teacher and Parent Rating Scales and Comparison Based on Birth Complication

Hypoxia	n	Hyperactivy criterion score*	Attention-Deficit criterion score*	ADHD Total criterion score*	ADDBD criterion score	Conners' teacher rating scales score	Conners' parent rating scales score
no	255	4.76 ± 3.4	4.69 ± 2.9	9.46 ± 5.9	16.56 ± 5.2	36.8 ± 11.3	58.76 ± 15.0
yes	15	5.87 ± 2.9	6.47 ± 2.4	12.33 ± 4.9	18.33 ± 4.3	43.13 ± 12.5	64.53 ± 12.4
Type of labor							
Spontaneous	217	4.76 ± 3.5	4.71 ± 2.9	9.47 ± 5.9	16.61 ± 5.2	36.08 ± 11.4	59.17 ± 15.2
C/S	44	5.30 ± 3.0	5.23 ± 2.9	10.52 ± 5.6	16.52 ± 5.2	39.77 ± 11.3	59.77 ± 13.1
Intervention	9	4.22 ± 3.3	4.56 ± 1.4	8.78 ± 4.4	18.33 ± 4.3	38.33 ± 12.1	53.78 ± 18.0
Pregnancy							
Planned	209	4.94 ± 3.4	4.96 ± 2.8	9.90 ± 5.7	16.77 ± 5.3	37.19 ± 11.3	59.40 ± 15.0
Unplanned	61	4.43 ± 3.5	4.21 ± 3.0	8.64 ± 6.3	16.26 ± 4.9	35.28 ± 11.7	58.02 ± 14.7
Duration of pregnancy							
Preterm	25	5.44 ± 3.6	5.28 ± 3.1	10.72 ± 6.4	16.44 ± 5.5	37.92 ± 12.6	62.04 ± 18.1
Term	233	4.74 ± 3.4	4.74 ± 2.9	9.48 ± 5.8	16.59 ± 5.1	36.55 ± 11.3	58.71 ± 14.3
Postterm	12	5.17 ± 3.4	4.75 ± 2.8	9.92 ± 5.8	18.42 ± 5.9	38.33 ± 13.3	60.25 ± 19.6

C/S : Cesarean section.
ADHD: Attention-deficit hyperactivity disorder.
* According to the sum of DSM-IV attention-deficit/hyperactivity disorder diagnosis criterion items.

Table VI. Conners' Teacher-Parent Rating Scales and ADDBD-ADHD Score of Patients With or Without Hypoxia

Diagnosis		n	ADDBD score*	ADHD score**	Conners' teacher rating scales score	Conners' parent rating scales score
ADHD	hypoxia –	111	18.43 ± 4.38	14.64 ± 2.58	39.22 ± 11.60	59.17 ± 16.23
	hypoxia +	10	19.17 ± 3.54	14.17 ± 2.66	44.17 ± 11.38	64.08 ± 11.67
ODD	hypoxia –	47	15.80 ± 6.22	7.07 ± 4.90	34.38 ± 12.33	55.07 ± 17.52
	hypoxia +	3	18.67 ± 4.73	9.33 ± 3.79	38.67 ± 16.65	68.33 ± 6.51
CD	hypoxia –	97	14.72 ± 4.99	4.63 ± 3.88	34.08 ± 9.90	59.96 ± 12.10

ADDBD: Attention-deficit and disruptive behavior disorders.

* According to the sum of DSM-IV attention-deficit/hyperactivity disorder (ADHD)+ conduct disorder (CD) and oppositional defiant disorder (ODD) diagnosis criteria items.

** According to the sum of DSM-IV attention-deficit/hyperactivity disorder diagnosis criteria items.

Discussion

When researching the risk factors related to ADHD and other disruptive behavioral disorders, may of the previous reports indicate mostly the relation between prematurity and birth weight. McCormick et al.[30] examined three preterm groups: very low birth weight (VLBW) (< 1500 g), low birth weight (LBW) (1500-2500 g) and normal birth weight (NBW) (over 2500 g), ranging in age from five to 17 years at follow-up. They concluded that VLBW and hyperactivity contribute independently to academic problems. Parents and teachers rate British children born weighing less than 1,250 g as more overactive, more easily frightened and clumsier than their classmate controls[31]. When the groups in our study were compared regarding parent and teacher rating scores, although parents' ratings were higher than those of the teachers, there was no significant difference. There was also no significant difference when grouped according to the presence of birth complications and type of delivery. In terms of prematurity, the most common predictable behavioral problem appears to be ADHD. In general, studies have indicated that somewhere between 5-35% of premature children have characteristics consistent with ADHD[27]. In our sample population, we could not identify any difference between groups in terms of the defined criteria or the rating scales of teachers and parents; the data was not statistically significant.

To determine the prevalence of disruptive behavior disorders in LBW infants (BW ≤ 200 gr), Pharoah et al.[32] studied 233 matched case-control pairs attending normal primary school and 36 unmatched children attending a special school. On the parental questionnaire screen 36% of the cases and 22% of the controls had a behavior disorder, and on the teacher questionnaire this ratio was 27% and 12%, respectively. Hyperactivity was more common among males than their control (21% versus 5%). O'Callaghan[33] also showed that although the prevalence of ADHD was not increased in ELBW children, they experienced marked problems in reading, spelling, mathematics, and writing when compared to control children. They were nearly three times more likely to be delayed by more than a year in all aspects. Milberger et al.[34] evaluated the role of pregnancy, delivery and infancy complications in the etiology of ADHD and showed positive associations. Moreover, those complications were associated with the correlates of ADHD, such as impaired cognitive functioning and poor school performance.

Since we did not use a control group in our study, the main purpose was to investigate any differences between subgroups of ADHD and other disruptive behavior disorders with regards to pre-and perinatal factors. Analysis of the existing data showed no significant difference between the groups in terms of the defined criteria except for history of unwanted pregnancy among patients in the conduct disorder group (32.3%). This result can be interpreted in two ways: either children with CD are born to mothers with an unwanted pregnancy, or those children are so troublesome that parents may think that the pregnancy was unwanted. Although our study is a retrospective evaluation in an ongoing large study, we can postulate that these pre-and perinatal events, prematurity, low birth weight, and hypoxia-related complications, may also be risk factors for ODD and CD, as well as for ADHD. ODD and CD patients could also be at risk for a range of developmental disabilities seen in patients with ADHD.

We recognize that a firm conclusion cannot be reached on this subject in view of the small number of patients in our study, without also thoroughly examining family dynamics, socioeconomic factors, and home environment,

and without following/evaluating the children to adulthood. Our aim was just to relate findings from a new non-investigated point of these disorders; i.e. risk factors occurring very early in life. This new perspective will hopefully provide the pediatrician, child psychiatrist, neonatologist, and psychologist with a better understanding of the disorders and aid their efforts in intervention.

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