Prenatal and Early Postnatal Exposure to A Natural Disaster and Attention-Deficit/Hyperactivity Disorder Symptoms in Indian Children

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Research Article

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Abstract

The aim of this study was to assess the relation between early exposure to stressful event and a level of Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms in children, based on outcomes from a natural experiment. It was hypothesized that children pre- and postnatally exposed to cyclone Aila have a higher level of ADHD symptoms compared to the controls, and the effect depends on timing of exposure. Indian children (8-11y) prenatally (N=336) and early postnatally (N=216) exposed to Aila were compared to non-exposed control group of their peers (N=285). ADHD symptoms were assessed using the Conner's Teacher Rating Scale Revised. The main effect of exposure to the cyclone on total ADHD symptoms' score, ADHD index, Hyperactivity and Oppositional symptoms was significant and independent of covariates. Both prenatally and postnatally exposed girls, and only postnatally exposed boys, showed significantly higher level of Oppositional symptoms compared to the controls. Cognitive problems/Inattention symptoms were increased in both prenatally and postnatally exposed boys, but not girls, compared to non-exposed children. The timing of programming the later behavior characteristics by stressful experiences due to natural disaster is not limited to fetal life but extends at least into infancy. Sex is a significant modulator of the early stress-ADHD symptoms association.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by age-inappropriate levels of inattention, hyperactivity and impulsivity [1] and affects the life of patients by increasing significantly the risk of academic failures, conflicts with peers and family members [2]. Lower occupational level [3], higher rates of unemployment [4], physical injures and early life mortality [5] are among the adverse life outcomes associated with ADHD. It is, therefore, considered a life-long disorder bearing a high cost for the patients, as well as for the society.

In addition to genetic risk factors, environmental risk factors contribute to the development of ADHD. One of the prenatal factors that may affect child's neurodevelopment and increase later risk of ADHD is early stress experience. Previous studies found the risk of ADHD related to the exposure of mothers to stressful events during pregnancy [6, 7, 8] and to high level of perceived prenatal maternal stress (PNMS) [7]. Moreover, also the stressful adverse experiences in early postnatal life were found to be associated with the probability of ADHD diagnosis in children [9, 10, 11].

The connection between behavioural symptoms and early environmental stress is complicated by the type of stressors assessed. It has been found that the adverse experiences causing prenatal and postnatal stress are to a varying degree dependent on the genetically influenced behavioral tendencies. Thus, their effects on a child's development could not always be conceived as pure effects of environmental factors [8]. Another problem with the interpretation of the relation between ADHD and early stress is that a cause of prenatal stress is likely to persist at least into the early postnatal life of a child and affect home environment, further disrupting the development of behavioural control [7]. Thus, the symptoms of ADHD may be the effect of accumulation of both pre- and postnatal exposure to a stressor. Based on these observations, it can be concluded that studies on the relation between early stress and ADHD symptoms should be controlled for genetic factors, e.g., by including independent adverse events, such as natural disaster [8], and also for the timing of exposure to stress.

While considering all the above-mentioned suggestions, the aim of the research was to assess the relation between early exposure to independent stressful event and a level of ADHD symptoms in children. The study was based on outcomes from a natural experiment. Possible consequences of severe cyclonic storm Aila, which affected coasts of Bangladesh and India in 2009, on ADHD symptoms have been assessed. We hypothesized that Indian children pre- and postnatally exposed to the natural disaster have a significantly higher level of ADHD symptoms in the preadolescent period compared to the control group of children non-exposed to the severe cyclone Aila, and the effect will depend on timing of exposure.

Materials And Methods

Ethical statement

Ethical approval for the research was obtained from the Institutional Ethics Committee for Research on Human Subjects, West Bengal State University, West Bengal, India (approval no. WBSU/IEC/14/03, dated 13.11.2017). The research was conducted in accordance with Helsinki Declaration and The Protection of Children from Sexual Offences Act of India. The data were collected from the eligible children and their mothers. Only children whose parents or legal guardians provided written informed consent were included in the study.

Funding

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Aila: the severe cyclonic storm

A tropical cyclone called *Aila* hit India and Bangladesh at a speed of 120-140 km per hour, between May 23 to May 26 2009, and devastated the coastal islands of the Sunderbans, the largest delta in the world. According to the India Meteorological Department, it was classified as 'severe cyclonic storm' [12]. It claimed 138 human- and uncountable cattle lives and human properties [13, 14]. Scientific studies conducted so far to portray the aftermath of the cyclone have mainly focused on the ecological [12, 15] and economical effects [16], livelihood and resilience [17], on the post-disaster health hazards, such as an increased number of diarrhea cases and cholera outbreak and on the psychological impacts on the adult population [18]. One earlier study reported the impact of the Aila cyclone on nutritional and weight status of Indian mother-child dyads [19].

Study area and Participants

The study included three groups of children (1) AilaPreS (prenatal exposure to the Aila-related stress): recruited from the two islands of the Sunderban area most affected by the cyclone. These children were intrauterine during the cyclone and born between June 2009 and February 2010, (2) AilaPostS (postnatal exposure to the Aila-related stress): the children who lived in the same areas as AilaPreS but were born up to 2 years before Aila and faced all the post-disaster hazards during their infancy, and (3) the control group belonged to the same birth cohort as AilaPreS, i.e., intrauterine during the cyclone and born between June 2009 and February 2010. They were recruited from the villages of the neighboring district that did not face the cyclone.

AilaPreS and AilaPostS groups came from two islands of the Sunderban delta region, called Satjelia and Kumirmari, in the district of South 24 Parganas and under the community development (CD) block, called *Gosaba*. These were the most affected islands, in terms of severity of the damage due to the cyclone. Children of AilaPreS and AilaPostS groups were recruited from 22 schools in Satjelia Island and 13 schools in Kumirmari Island. The control group of participants were recruited from 21 schools in the rural Eastern part of the adjacent district, North 24 Parganas, under the CD Block, Bongaon.

Assessment of ADHD symptoms

A level of ADHD symptoms among children was assessed by class teachers using the Conner's Teacher Rating Scale Revised (short version) (CTRS-R:S) [20]. The Conner's questionnaires belong to the most widely used child behaviour ratings scales in the world [21], including India [22, 23, 24]. The symptoms were assessed using the total score of CTRS-R:S and 4 indexes: Cognitive problems/inattention index, Hyperactivity index, Oppositional symptoms index and ADHD index, which is a combination of items derived from empirical discrimination between clinical and matched control cases [20]. Sum of scores for each index as well as for all items was used for the purpose of statistical analysis.

Controlled factors

The symptoms of ADHD vary between males and females in terms of severity and subtypes [25]. Thus, we assumed that sex could also act as a significant modulator of the Aila exposure-ADHD symptoms link and included this factor to the analysis as a control variable.

The level of maternal stress related to adverse life experiences which occurred during last year before the time of the study was assessed by the Holmes and Rahe Stress Scale (HRSS), also known as the Social Readjustment Rating Scale [26]. The questionnaire is a list of 43 stressful life events called a Life Change Units. Each of them has a different 'weight' for stress. The higher number of stressful events and the larger the weight of events, the higher is the level of stress.

ADHD has been previously found to be related to low socioeconomic status of a family [27] and, based on previous reports from the region [17], we assumed that socioeconomic status (SES) of a family was acutely affected by natural disaster. Previous studies showed that among inhabitants of the same area, the impact of psychological trauma following cyclone Aila had differentially affected people from different socio-economic strata, the lower class being the worst affected [18]. Thus, SES was controlled in the statistical analyses of the present study. The monthly family income per capita for each family was calculated by dividing the monthly family income by the number of family members. Education of each parent was also recorded as the highest level they passed from educational institutions and was categorised into three groups: non-literate, up to primary level, and up to secondary level, for the purpose of analysis.

The risk of ADHD was found to be related to perinatal factors [28]. Because such characteristics as gestational age and birth weight may be mediators between prenatal stress and ADHD and may be confounding factors in the link between postnatal stress and ADHD, they were also included in the analysis as covariates.

Statistics

Differences between the three groups were assessed by one-way analysis of variance (ANOVA) in case of normally distributed dependent variable. However, for the dependent variables which were not normally distributed, Kruskal-Wallis test was performed. Differences between sexes within each group were assessed by student t-test for independent samples. Differences in scores of ADHD and Oppositional symptoms between exposed groups and control group within each sex were assessed by ANOVA, and *post-hoc* comparisons were done by the Dunnett's test. Differences in distribution in appropriate categories of parental education were assessed by Pearson's chi-square test. Effects of exposure to Aila cyclone were assessed by multiple analysis of covariance applied by Generalized Linear Model (GLM) with logit link function. Two GLM models of this analysis were performed, depending on the number of confounding factors that were included. In the model I, scores of ADHD and Oppositional symptoms were dependent variables, while groups (AilaPreS, AilaPostS and control group) and sex were the independent variables and age was a covariate. In the model II the following variables were included as the covariates: age, fathers' and mothers' education levels (in three categories each), mothers' HRSS, family income per capita, gestational age at birth and birth weight. The second-order interaction effect between group and sex was additionally included in both models. The significance of the effects was assessed by Wald's chi-square, while the effect size was reported using odds ratio (OR). On all graphs, the results of *post-hoc* comparisons between groups were included. The required significance level was assumed at $p<0.05$. All calculations were performed in Statistica 13.1.

Results

This study included 837 children. Among them 336 children were included to the AilaPreS group, 216 children to the AilaPostS group and 285 children to the control group. However, due to lack of other parental and birth information the numbers differed depending on analysis and is reported in each table. Two main statistical GLM models I and II included

802 and 524 children, respectively. However, the children who dropped out from the main analysis did not significantly differ in most of CTRS-R:S indices, except for the higher Cognitive problems/inattention symptoms ($p<0.05$).

Descriptive statistics of confounding factors by sex and group are shown in Table 1. In both sexes, there were significant differences in mean age between groups, with expected older age of children in AilaPostS in comparison with two other groups. Members of three groups significantly differed in mother's level of education. Most of the non-literate mothers were in AilaPostS (23%), whereas the most of mothers with the at least secondary education were found in the control group (34%). Groups did not differ in father's education level. The highest mean income *per capita* was noted for the control group, whereas the lowest for AilaPostS group. Mothers of children from AilaPreS had the highest scores of HRSS, in comparison to mothers of members of two other groups ($H=344.41$, $p<0.001$). Mean birth weight did not show significant differences between groups, but gestational age was significantly the highest in controls, followed by AilaPreS and AilaPostS group ($F=12.45$, $p<0.01$).

Descriptive statistics of CTRS-R:S scores for groups by sex are presented in Table 2. In boys, all CTRS-R:S indexes showed significant differences between groups (at least $p<0.01$). The highest values of scores for all indices were found in AilaPostS group and followed by AilaPreS. Similar results were obtained for girls, with the exception of insignificance of the between-group differences in Cognitive problems/inattention index.

Within the three groups, there were significant sex differences in CTRS-R:S indices. Total score, ADHD index and Hyperactivity index differed significantly between boys and girls from AilaPreS group ($p<0.001$) to the disadvantage of boys. Similarly, within AilaPostS and control group, in all CTRS-R:S indices boys showed significantly higher scores than girls (at least $p<0.05$), except for Cognitive problems/inattention.

Results of the analysis of covariance have shown a significant effect of group (AilaPreS, AilaPostS and control group) on all CTRS-R:S indices (at least $p<0.05$) in both analysed models, independently from sex, controlling the age in a model I and the number of confounders in a model II (Table 3). All effects of second-order interactions between group and sex were not significant pointing out that these two factors acted independently. The effect size assessed by OR (control group as a reference) indicated an increased risk of higher scores of all CTRS-R:S indices in the Aila-exposed groups in a range from OR=1.03 to OR=1.23 (except for Cognitive problems/inattention score in AilaPostS group in both models, where OR=0.99, and Hyperactivity score in AilaPreS group in model II, where OR=0.99; Table 3). The highest ORs were found for Hyperactivity index and AilaPostS in both model I and II (OR=1.20 and OR=1.23 respectively)

Means with confidence intervals and results of *post-hoc* comparisons between the two exposed groups and control, for all ADHD indices, are shown on Figure 1a-e. Both in boys and girls, the highest total scores of CTRS-R:S were found in AilaPostS, however, the means of both exposed groups significantly differed from the control group (Fig. 1a). The same pattern appeared in case of the ADHD index (Fig. 1b) and Hyperactivity (Fig. 1c). Means of Cognitive problems/inattention score were significantly different between exposed groups and the control group in boys, but not in girls (Fig. 1d). In boys, only the AilaPostS group showed a significant difference in comparison to the control group in a mean score of Oppositional symptoms, whereas in girls both AilaPreS and AilaPostS showed significant differences in this parameter compared to the control group (Fig. 1e).

Discussion

This study examined the effects of early exposure of children to the severe cyclonic storm Aila on the later level of ADHD symptoms. Till date, a few research projects, as the 1998 Quebec Ice Storm, Canada [29, 30], the Iowa Flood Study in USA [31] or the Queensland Flood (2011) Study in Australia [32], utilized natural disaster as a design for investigating the impact of prenatal stress on child development. Nevertheless, to the best of our current state of knowledge, we are presenting the first study examining the ADHD symptoms as associated with the exposure to natural disaster, and with a control of the timing of exposure (pre- vs. early postnatal).

The most important result we have obtained is that both pre- and early postnatal exposure to severe objective and independent adverse event was significantly associated with the increased level of ADHD symptoms in preadolescent children compared to a control group. It is consistent with the results of previous research, conducted with diversified methodology, on the effects of prenatal [7, 8] and postnatal stress [9, 10, 11] on ADHD symptoms in later life. Biological mechanisms have been proposed to explain how adverse experiences affect child's development. Increased maternal glucocorticoids resulting from PNMS might impair intrauterine blood flow, affecting child's neurodevelopment leading to cognitive and behavioural consequences in later life [33]. Extensive brain growth and development occur also during the first two years of postnatal life. Research from both animal models and humans suggest that stress occurring during the first months of life may be particularly influential for neurodevelopmental outcomes [34].

Because parental education and income [27] as well as characteristics of birth and newborns [28] were previously found to be associated with ADHD, they could be also significant modulators of the stress-ADHD link in our study. However, the detailed analyses unravelled the fact that the main effect of exposure to a natural disaster on the summed score of CTRS-R:S (total ADHD), ADHD index, as well as Hyperactivity and Oppositional symptoms were independent of these factors. Less clear results were obtained for Cognitive problems/inattention. These symptoms were related to early life stress only in boys and when the analysis was not adjusted for other covariates. The *post-hoc* analysis further revealed some other sex-specific patterns of the associations. Different effects of prenatal stress on the ADHD symptoms in boys and girls were found also in other studies [35]. These outcomes might be a result of biological differences between sexes in the vulnerability of the dopamine transmitter system, the binding ability of the serotonin receptor 5-HT1A in the hippocampus, hypothalamic-pituitary-adrenocortical axis and the neurotrophic effect of sex hormones [35]. Some of these explanations may also be extended in case of early postnatal stress, although confirmatory studies are warranted.

Although we have included several potentially confounding variables in our study, there could be a few other important factors that were not controlled. For example, we did not record factors such as maternal social support system and differential coping with stress strategies which might have important modulating effects on childhood ADHD symptoms [35]. Besides, the present study did not consider other possible adverse experiences that might have occurred during the later childhood development after the Aila cyclone. Thus, the link between the exposure to Aila and ADHD symptoms might have emerged as well through the accumulation of the effects of other plausible Aila-dependent or independent stressors (both biological and psychosocial) in the post-Aila phase of life. For example, several cases of diarrhea were noticed due to food and water contamination following Aila cyclone rather than the storm itself. This suggests a possibility the observed relation between the exposure to natural disaster and ADHD symptoms may be connected to diet, microbiota and gut-brain axis. Although the latest review on the relation between microbiota and ADHD symptoms revealed no clear conclusion on their association [36], it remains probable that diet, food contamination and pathogenic bacteria in a sensitivity window may affect brain development and cause later behavioral and cognitive symptoms. These factors were not controlled in our research.

Conclusion

The study was aimed to examine the association of prenatal and early postnatal exposure to a severe natural disaster with the level of ADHD symptoms in children. The results showed that an increase in externalizing symptoms was related with an exposure to the cyclonic storm, Aila. The ADHD symptoms in the Aila-exposed children might be interpreted as the effect of stress-induced modifications in nervous system occurring as early as in prenatal period. Nevertheless, the study suggests the programming effect of stressful experience is not limited to fetal life but extends at least into infancy. The effects of early stress were found to be independent of socioeconomic status and newborns' characteristics, and partially modulated by sex. Future research on the possible epigenetic, neurobiological and psychosocial mechanism linking early stress, particularly due to severe ecological disasters, and later behavioral symptoms is warranted.

Declarations

Authors' contributions: T.H. analyzed the data, interpreted the results, wrote the main manuscript text. A.G. and N.N-S. edited the database, provided critical comments and edited the manuscript for intellectual content. R.C. supervised the data collection, prepared database and revised the manuscript. S.K. organized, arranged and coordinated the study, analyzed the data, prepared figures and tables and provided critical comments. All authors reviewed and approved the manuscript.

Data availability: The dataset analysed during the current study is available from the corresponding author on reasonable request.

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Competing interests: The authors declare no competing interests.

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Tables

Table 1. Descriptive statistics of all confounding variables by groups

	AilaPreS	AilaPostS	Control	
Age				
N; mean (SD)				
Boys	175; 8.06(0.21)	109; 9.31(0.50)	142; 8.31(0.23)	F=543.4***
Girls	161; 8.08(0.24)	107; 9.28(0.36)	143; 8.32(0.23)	F=647.9***
Mother's education				
N (%)				
No educated	15(5)	41 (23)	30 (11)	
At most primary	197 (67)	116 (65)	147 (55)	
At most secondary	83 (28)	21 (12)	91 (34)	χ^2=54.01***
Father's education				
N (%)				
No educated	48 (15)	27 (15)	42 (16)	χ^2=4.60 n.s.
At most primary	168 (52)	101 (57)	125 (47)	
At most secondary	105 (33)	50 (28)	98 (37)	
Income per capita (INR)				
N; mean (SD)	300; 1207(1090)	177; 844 (586)	263; 1666 (1203)	H=130.77***
Scores of last year mother's stress (HRSS)				
N; mean (SD)				
	295; 335 (136)	152; 117 (130)	228; 92 (84)	H=344.41***
Gestational age (weeks)				
N; mean (SD)	311; 38.0 (2.3)	148; 37.6 (2.7)	257; 38.8 (2.7)	F=12.45***
Birth weight (g)				
N; mean (SD)	261; 2662 (524)	150; 2678 (479)	239; 2749 (545)	F=1.87 n.s.

*** p<0.001, n.s.- non-significant, AilaPreS – prenatally Aila-exposed children, AilaPostS - postnatally Aila-exposed children, Control – non-exposed to Aila counterparts. H – the result of Kruskal-Wallis test, F - F-statistic from ANOVA test, χ^2 – value of the Pearson's' chi square test.

Table 2. Descriptive statistics of CTRS-R:S indices in AilaPreS, AilaPostS and control group. Differences were assessed by one-way ANOVA, and sex differences were assessed by t-Student test for independent samples (marked only significant p – level).

	AilaPreS			AilaPostS			Control group			ANOVA for differences between groups	
	N	mean	SD	N	mean	SD	N	mean	SD	F	P
Boys											
CTRS-R:S total	170	35.1	16.8	101	37.9	14.9	137	28.9	17.9	9.28	0.001
ADHD index	173	14.3	6.8	105	15.3	6.0	139	11.6	7.4	10.17	0.001
Cognitive problems/ Inattention	171	7.1	4.4	107	7.7	3.6	141	6.0	3.8	5.93	0.01
Hyperactivity	173	8.8	4.6	108	9.3	4.1	142	7.3	5.2	6.84	0.001
Oppositional symptoms	172	4.5	3.3	107	5.5	3.1	142	3.9	3.9	7.09	0.001
Girls											
CTRS-R:S total	161	29.1[c]	14.6	98	30.3[b]	15.1	140	22.3[c]	17.3	9.90	0.001
ADHD index	161	11.7[c]	6.0	104	12.4[b]	6.1	140	8.9[c]	7.0	10.82	0.001
Cognitive problems/ Inattention	161	6.4	4.0	106	6.8	3.7	140	5.8	4.0	2.21	n.s.
Hyperactivity	161	6.4[c]	4.1	104	7.0[c]	3.7	140	4.6[c]	4.5	11.40	0.001
Oppositional symptoms	159	4.3	3.1	104	4.2[a]	3.4	141	2.7[b]	3.4	10.16	0.001

AilaPreS – prenatally Aila-exposed children, AilaPostS - postnatally Aila-exposed children, Control – non-exposed to Aila counterparts, F - F-statistic from ANOVA test, p – the level of significance of result, a, b and c – intragroup statistically significant differences between girls and boys: a – $p<0.05$, b – $p<0.01$, c – $p<0.001$

Table 3. Results of Generalised Linear Model (GLM), where CTRS-R:S indices were dependent variables, and groups (AilaPreS, AilaPostS, Control group) and sex were independent variables. Model I included only age as a covariate, whereas Model II included several confounders: age, parental education, family income, mother's HRSS score, gestational age and birth weight.

	CTRS-R:S total score		ADHD index		Cognitive problems/Inattention		Hyperactivity		Oppositional symptoms	
	Wald's χ^2	OR (±CI)	Wald's χ^2	OR (±CI)	Wald's χ^2	OR (±CI)	Wald's χ^2	OR (±CI)	Wald's χ^2	OR (±CI)
	Model I N=802									
Group	28.83***		31.12***		10.46**		29.16***		20.96***	
AilaPreS		1.09 (1.01-1.17)		1.09 (1.01-1.18)		1.10 (1.01-1.19)		1.03 (0.94-1.13)		1.07 (0.96-1.20)
AilaPostS		1.08 (0.98-1.19)		1.08 (0.98-1.19)		0.99 (0.89-1.10)		1.20 (1.07-1.34)		1.17 (1.02-1.36)
Sex	32.23***		32.86***		4.69*		57.40***		14.00***	
Group x Sex	0.61		0.41		0.64		1.96		5.38	
	Model II N=524									
Group	12.56**		15.28***		6.22*		12.85**		10.49**	
AilaPreS		1.08 (0.96-1.21)		1.07 (0.96-1.20)		1.12 (0.87-1.27)		0.99 (0.87-1.12)		1.13 (0.95-1.33)
AilaPostS		1.09 (0.95-1.25)		1.12 (0.97-1.28)		0.99 (0.85-1.15)		1.23 (1.05-1.43)		1.12 (0.91-1.36)
Sex	19.60***		19.11***		1.35		36.20***		10.68***	
Group x Sex	0.88		0.68		0.13		1.18		3.72	

AilaPreS – prenatally Aila-exposed children, AilaPostS - postnatally Aila-exposed children, Control – non-exposed to Aila counterparts, OR – odds ratio, ±CI – 95% confidence interval for odds ratio, ***p<0.001, **p<0.01, *p<0.05

Figures

Figure 1a

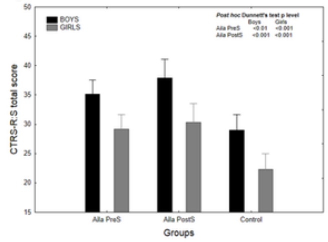

Figure 1b

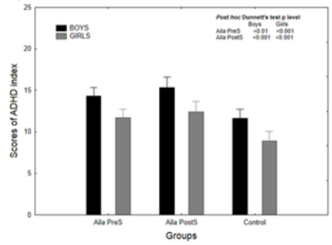

Figure 1c

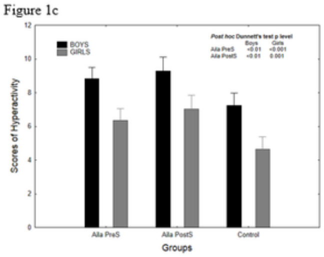

Figure 1d

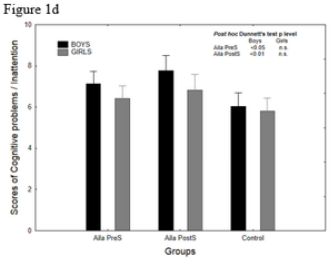

Figure 1e

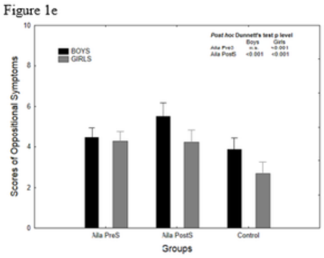

Figure 1

a-d. Means, CIs (confidence intervals) and Dunnett's test results for total scores of CTRS-R:S (a) ADHD Index (b) Hyperactivity (c) Cognitive problems/inattention (d) and Oppositional symptoms (e) in boys and girls by two groups of Aila-exposed children and controls.