

Age and Sex Analyses of Somatic Complaints and Symptom Presentation of Childhood Depression in a Hungarian Clinical Sample

Ildikó Baji, MD; Nestor L. Lopez-Duran, PhD; Maria Kovacs, PhD; Charles J. George, MS; László Mayer, MD; Krisztina Kapornai, MD; Enikő Kiss, MD; Julia Gáboros, MD, PhD; and Ágnes Vetró, MD, PhD

Objective: To determine whether the symptom presentation of major depressive disorder (MDD) in a large clinical sample of youngsters is influenced by age, sex, and the interaction of age and sex.

Method: The sample included 559 children (mean age = 11.69 years; range, 7–14 years; 247 girls) with MDD recruited from 23 mental health facilities across Hungary. Psychiatric evaluations were conducted via the semistructured Interview Schedule for Children and Adolescents-Diagnostic Version (ISCA-D). Final *DSM-IV* diagnoses were rendered via the best-estimate diagnostic procedure. Evaluations were conducted between April 2000 and May 2005.

Results: Six depression symptoms increased with age: depressed mood (odds ratio [OR] = 1.10, $P < .05$), hypersomnia (OR = 1.17, $P < .05$), psychomotor retardation (OR = 1.11, $P < .05$), fatigue (OR = 1.13, $P < .01$), thoughts of death (OR = 1.11, $P < .05$), and suicidal ideation (OR = 1.18, $P < .01$), while psychomotor agitation decreased with age (OR = 0.91, $P < .05$). Boys were less likely to evidence anhedonia (OR = 0.67, $P < .05$), insomnia (OR = 0.68, $P < .05$), and hypersomnia (OR = 0.56, $P < .05$) but more likely to have psychomotor agitation (OR = 1.59, $P < .01$). There were no age-by-sex interactions. Rates of somatic complaints did not decrease with age (OR = 1.01, $P > .05$).

Conclusions: The symptom presentation of MDD becomes somewhat more neurovegetative as children get older. However, girls display more affective and atypical symptoms across all age groups. Somatic complaints were common regardless of age and should be considered an associated feature of depression in children and adolescents.

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Over the past 3 decades, a large body of research has shown that children and adolescents can meet diagnostic criteria for major depressive disorder (MDD) as defined in standard diagnostic manuals (eg, *DSM-IV*; see review by Birmaher et al¹). However, questions have remained about the appropriateness of such criteria for younger age groups. Most questions concern 2 issues, namely, (1) Are *DSM* criteria for MDD able to accommodate age-related differences in the likelihood of particular symptoms? and (2) Are there different symptoms associated with MDD as a function of a child's age, sex, and age-by-sex interactions? Surprisingly, research on age and sex differences in depressive symptomatology with clinical populations is scarce, and our current understanding of these effects is mostly based on studies using small sample sizes that limit the identification of subtle effects.

A small number of studies have examined developmental differences in rates of specific symptoms across depressed children and adolescents. For example, Ryan et al² reported that, compared to depressed children, adolescents with MDD were more likely to display hopelessness, hypersomnia, and weight gain/loss and less likely to display somatic complaints and psychomotor agitation. In a similar study, Yorbik et al³ found that depressed adolescents displayed significantly higher rates of hopelessness/helplessness, fatigue, lack of energy/tiredness, hypersomnia, weight loss, and suicidality than depressed children. However, Mitchell et al⁴ found hypersomnia to be the only symptom more frequent in clinically depressed adolescents than in depressed children. Discrepant findings may be related to significant methodological differences between the studies. For example, Mitchell and colleagues⁴ study was conducted with a small sample of inpatient youth, while the studies by Ryan et al² and Yorbik et al³ had larger samples of outpatient children and adolescents.

Given that somatic symptoms have been historically viewed as a common presentation of childhood depression,⁵ several studies have examined the association between somatic complaints and depression in younger ages,^{4,6} but they have yielded contradictory findings. For example, some researchers reported more somatic complaints among

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Corresponding author: Nestor L. Lopez-Duran, PhD, University of Michigan, Department of Psychology, 530 Church St, 2253 East Hall, Ann Arbor, MI 48109 (nestorL@umich.edu).

prepubertal children compared to postpubertal children,² while others failed to find this developmental difference.⁴ Such discrepant findings may reflect that none of these studies have controlled for comorbid anxiety that could have affected the results given the high rates of anxiety disorders among depressed youths (eg, Kovacs⁷) and the strong association between somatic symptoms and anxiety in childhood.⁸

All in all, extant studies of age-related differences in symptom presentation among clinically depressed pediatric samples suggest that adolescents tend to have more vegetative symptoms than children, yet there is no clear picture regarding differences in specific symptoms during various ages. Furthermore, previous examinations of age differences have used pubertal status (prepubertal versus postpubertal) to subdivide the samples. Examining chronological, age-related changes in symptom presentation continuously, rather than categorically, may reveal more subtle developmental effects on symptom presentation throughout middle childhood and adolescence.

Examinations of sex differences in child and adolescent depression have generally focused on rates of diagnosis and severity of symptoms,^{9,10} with only a few studies of rates of specific symptoms. For example, Mitchell et al⁴ found no sex differences in rates of various depressive symptoms in a small sample of inpatient children and adolescents with MDD. Similarly, Roberts et al¹¹ failed to find sex differences in symptom presentation in a small community-based sample of adolescents meeting criteria for major depression. However, studies with larger samples have reported sex differences in appetite and weight fluctuations. For example, Williamson et al¹² found higher rates of weight gain among depressed girls compared to boys. Similarly, Yorbik et al³ reported that girls with MDD had higher rates of increased appetite than boys, but this effect was only observed among adolescents. Ryan et al,² however, failed to find sex differences in weight gain or appetite changes, although they found that preadolescent boys experienced more fatigue symptoms than preadolescent girls. These inconsistent findings may be due to significant differences in sample sizes and possible cohort effects, as studies differed greatly in the decade of data collection.

Therefore, in the present study, we sought to further our understanding of developmental changes in the symptomatology of childhood-onset depression using a uniquely large clinical sample of depressed children and adolescents in Hungary. Our first aim was to examine developmental differences in depressive symptom presentation using age as a continuous variable. Our second aim was to examine sex differences, as well as sex-by-age effects, in symptomatology. In addition to depressive symptoms, we also assessed age and sex differences in the presence of somatic complaints, given the reported high rates of somatic symptoms among depressed children.^{6,13} Further, given that there is overlap in some symptoms between depression and other

disorders (eg, anxiety, attention-deficit/hyperactivity disorder [ADHD]), we examined the effect of comorbid diagnoses on 2 symptoms: somatic complaints, and psychomotor agitation. Finally, our large sample allows us to use an advanced statistical method such as Alternating Logistic Regression (ALR),¹⁴ which is uniquely suited for simultaneously modeling multiple outcomes (eg, symptoms) while controlling for the possible intercorrelation between these outcomes.

METHOD

Participants

The sample included 559 children (247 girls) who were enrolled in a study of genetic and psychosocial risk factors for childhood-onset depression between April 2000 and May 2005. The mean age at evaluation was 11.69 years (SD = 2.00 years). Ethnic composition was representative of the ethnic composition of Hungary: 93.9% white, 3.6% gypsy (Roma), 2.3% multiracial, and 0.2% African. Subjects were recruited from 23 mental health facilities across Hungary. Children presenting at each site were selected for further assessment if they met the following criteria: 7.0 to 14.9 years old, no evidence of mental retardation, no evidence of major systemic medical disorder, availability of at least 1 biologic parent, and a 7–14.9-year-old sibling (required by the study's genetic component). Siblings are not included in this article.

Measures and Procedures

Enrollment and assessment procedures have been described in detail in previous publications.^{15,16} Children were screened for depressive symptoms by self-report and parental questionnaires. Those who scored above clinically established cutoffs received psychiatric interviews on 2 independent occasions administered by different trained psychiatrists/psychologists.

Clinical evaluations were conducted with the semistructured Interview Schedule for Children and Adolescents-Diagnostic Version (ISCA-D), an extension of the Interview Schedule for Children and Adolescents (ISCA).¹⁷ Each clinician interviewed the parent and the child separately and rendered an overall severity rating for each symptom. Good interrater reliability for symptom ratings has been reported.^{15,16} Final diagnoses were rendered by experienced psychiatrists using the best-estimate diagnostic procedure.¹⁸ Only those meeting criteria for MDD at the time of the evaluation were included in the present analysis. We examined the presence or absence of 16 *DSM-IV* criterion symptoms from the ISCA-D (see Table 1). We used clinicians' overall ratings and dichotomized them as clinically significant (entered into a given diagnosis) versus subclinical or absent.

Statistical Analysis

To estimate the effect of age, sex, and age-by-sex interactions on symptom presentation, we used ALR¹⁴ fitting a multivariate model of age and sex on the 16 symptoms of

**Table 1. Unadjusted Rates (%) of Depressive Symptoms Across Age Groups in Children With Major Depressive Disorder**

Symptom	Age at Interview, y								Statistic ^a (χ^2)
	7 (n=16)	8 (n=46)	9 (n=70)	10 (n=70)	11 (n=91)	12 (n=91)	13 (n=92)	14 (n=83)	
Depressed mood	63	61	66	69	73	60	73	81	5.04*
Irritability	75	76	80	83	86	79	73	81	NS
Anhedonia	38	43	49	40	43	48	51	43	NS
Weight loss	25	28	36	26	26	26	30	40	NS
Weight gain	6	28	21	26	26	16	24	14	NS
Insomnia	63	46	60	49	63	55	55	57	NS
Hypersomnia	13	11	6	10	11	14	17	23	9.33**
Psychomotor agitation	63	52	56	53	45	36	39	43	7.70**
Psychomotor retardation	31	30	34	29	37	46	39	47	6.49*
Fatigue	69	41	60	63	64	70	67	70	7.57**
Feelings of worthlessness	44	50	59	57	59	63	60	63	NS
Guilt	25	35	41	33	31	35	30	35	NS
Impaired decision-making	75	65	73	76	70	70	67	75	NS
Thoughts of death	44	35	59	61	55	68	55	65	6.69**
Suicidal ideation	25	17	34	39	41	44	45	49	13.87***
Somatic complaints	50	35	36	29	37	35	43	35	NS

^aMantel-Haenszel χ^2 , df=1.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

Abbreviation: NS = not statistically significant at nominal $\alpha < .05$.

interest. ALR is a type of Generalized Estimating Equation (GEE)¹⁹ that allowed us to simultaneously model the endorsement of each of the 16 symptoms while accounting for the possible intercorrelation of symptoms within participants. This method was initially created for analysis of intercorrelated cluster data²⁰ and has been extended to the analysis of intercorrelated outcomes.²¹

RESULTS

Unadjusted Rates of Specific Depressive Symptoms by Age and Sex

Table 1 presents the rates of endorsement of each symptom by age. Depressed mood, hypersomnia, psychomotor retardation, fatigue, thoughts of death, and suicidal ideation increased linearly with age. Psychomotor agitation was the only symptom that decreased linearly with age. Table 2 presents the rates of endorsement of each symptom by sex. Six symptoms were significantly more common in girls than boys, namely, depressed mood, anhedonia, insomnia, hypersomnia, psychomotor retardation, thoughts of death, and somatic complaints. In contrast, only psychomotor agitation was more commonly reported in boys than in girls.

Age and Sex Effects in Rates of Depressive Symptoms Adjusted for Intercorrelation Between Symptoms

Table 3 shows the adjusted odds ratio (AOR) of each symptom by sex and age while controlling for age, sex, and the correlation between symptoms. Results from the ALR indicated a significant effect of age ($\chi^2_{16} = 35.91$, $P = .003$) and sex ($\chi^2_{16} = 38.65$, $P = .001$). No age-by-sex interaction was observed, $\chi^2_{16} = 16.53$, $P = .42$. Consistent with the unadjusted results presented above and while controlling

Table 2. Unadjusted Rates (%) of Depressive Symptoms for Girls and Boys With Major Depressive Disorder

Symptom	Age at Interview, y		Statistic ^a (χ^2)
	Girls (n=247)	Boys (n=312)	
Depressed mood	74.1	65.4	4.90*
Irritability	77.7	81.1	NS
Anhedonia	51.0	41.0	5.55*
Weight loss	32.8	28.2	NS
Weight gain	22.3	20.8	NS
Insomnia	61.1	51.6	5.08*
Hypersomnia	18.2	9.9	8.05**
Psychomotor agitation	38.5	51.6	9.59**
Psychomotor retardation	43.7	34.0	5.47*
Fatigue	65.6	62.8	NS
Feelings of worthlessness	61.1	57.1	NS
Guilt	33.2	34.3	NS
Impaired decision-making	67.2	74.4	NS
Thoughts of death	62.8	54.2	4.17*
Suicidal ideation	43.7	36.5	NS
Somatic complaints	42.1	32.1	6.01*

^aMantel-Haenszel χ^2 , df=1.

* $P < .05$.

** $P < .01$.

Abbreviation: NS = not statistically significant at nominal $\alpha < .05$.

for sex and the intercorrelation between symptoms, the AOR of 6 symptoms increased with age, namely, depressed mood (10% increased odds per year), hypersomnia (17% increased odds per year), psychomotor retardation (11% increased odds per year), fatigue (13% increased odds per year), thoughts of death (11% increased odds per year), and suicidal ideation (18% increased odds per year). Only psychomotor agitation was more frequent in younger children (9% reduced odds per year). While controlling for age and intercorrelation between symptoms, being male significantly decreased the odds of 4 specific symptoms,

Table 3. Adjusted Multivariate Odds Ratios (95% CI) of Each Symptom Adjusted for Age and Sex via Alternating Logistic Regression^a

Symptom	Between-Subject by Symptom Effects	
	Age: Per Year	Sex: Male
Depressed mood	1.10 (1.01–1.21)*	0.71 (0.49–1.03)
Irritability	0.98 (0.88–1.10)	1.22 (0.80–1.86)
Anhedonia	1.01 (0.93–1.10)	0.67 (0.48–0.95)*
Weight loss	1.06 (0.96–1.16)	0.84 (0.58–1.22)
Weight gain	0.94 (0.85–1.03)	0.87 (0.58–1.31)
Insomnia	1.00 (0.92–1.09)	0.68 (0.48, 0.96)*
Hypersomnia	1.17 (1.02–1.35)*	0.56 (0.34–0.93)*
Psychomotor agitation	0.91 (0.83–0.99)*	1.59 (1.12–2.24)**
Psychomotor retardation	1.11 (1.01–1.21)*	0.71 (0.50–1.01)
Fatigue	1.13 (1.03–1.23)**	0.97 (0.68–1.39)
Feelings of worthlessness	1.06 (0.97–1.15)	0.88 (0.62–1.25)
Guilt	0.99 (0.90–1.08)	1.04 (0.72–1.49)
Impaired decision-making	1.02 (0.93–1.12)	1.43 (0.99–2.08)
Thoughts of death	1.11 (1.02–1.22)*	0.76 (0.54–1.08)
Suicidal ideation	1.18 (1.08–1.29)**	0.86 (0.61–1.21)
Somatic complaints	1.01 (0.92–1.10)	0.65 (0.46–0.93)*

^aNo sex-by-age interactions were noted.

* $P < .05$.

** $P < .01$.

namely, anhedonia (33% reduced odds), insomnia (–32%), hypersomnia (–44%), and somatic complaints (–35%), and significantly increased the odds ratio of psychomotor agitation (59% increased odds).

Finally, given the historical interest in whether somatic complaints may be a presenting symptom in pediatric depression, we examined its rate among children without comorbid anxiety disorder ($n = 398$). The rate of somatic complaints in this group was 29% on average (range, 20%–46% across all ages), a rate higher than other depressive symptoms such as hypersomnia and weight gain. Consistent with our full sample analysis, no age effects on somatic complaints were noted among children without comorbid anxiety ($\chi^2_1 = 0.53$, $P = .47$). However, the sex difference in somatic symptoms in the full sample did not remain significant after controlling comorbid anxiety disorder (33% in girls vs 26% in boys), $\chi^2_1 = 1.77$, $P = .18$. We also examined the rate of psychomotor agitation in children without comorbid ADHD ($n = 449$). Consistent with our full sample analysis, we found an age effect on psychomotor agitation (decreasing rates of agitation in older cases) even among children without comorbid ADHD ($\chi^2_1 = 7.19$, $P < .01$). Finally, also consistent with our full sample analysis, boys were more likely than girls to present psychomotor agitation after controlling for comorbid ADHD ($\chi^2_1 = 10.13$, $P < .01$).

DISCUSSION

In this study, we examined age and sex differences in rates of depressive symptoms in a uniquely large sample of children and adolescents diagnosed with MDD. Our large sample allowed for the simultaneous assessment of age and sex effects using ALR, which controls for possible intercorrelations of symptoms within participants and provides

robust, more reliable estimates than previously used methods. Our findings indicate significant sex and age differences in the presentation of several symptoms, but surprisingly, we did not find any age-by-sex interactions.

Consistent with previous studies,^{2–4} we found that several neurovegetative symptoms increased with age, including hypersomnia, psychomotor retardation, and fatigue. This pattern was accompanied by a significant increase in depressed mood, thoughts of death, and suicidal ideation and a reduction in rates of psychomotor agitation. Our results are consistent with Weiss and Garber's²² meta-analytic review in which they concluded that depression is not isomorphic in symptomatology or syndrome presentation throughout early development, despite some studies indicating that symptom presentation is relatively unchanged between children and adolescents (eg, Ryan et al²). Specifically, our results indicate that the presentation of depression becomes more neurovegetative as children transition from childhood into adolescence. Our findings are also consistent with Carlson and Kashani's²³ conclusions that depressed mood becomes more frequent with age. Yorbik et al³ also found an increase in rates of depressed mood in adolescence compared to childhood.

With regard to age effects, our findings are not entirely consistent with the *DSM-IV* criteria according to which irritability can substitute for depressed mood as a required symptom²⁴ in childhood. Specifically, depressed mood and irritability were relatively frequent across all ages, with more than 60% of patients displaying the 2 symptoms. In contrast, anhedonia was relatively infrequent across all age groups with rates generally below 50%. This suggests that anhedonia, not depressed mood, is the least frequent core symptom in depression among children and adolescents while irritability is significantly more common, occurring often in conjunction with, rather than as a substitute for, depressed mood.

Given that depression and ADHD share the symptom of psychomotor agitation and that there is a developmental trend in ADHD diagnostic rates (see Willoughby),²⁵ we examined whether the reduction in psychomotor agitation observed in depression in older children was due to age-related drops in ADHD comorbidity. We found that psychomotor agitation symptoms decreased significantly across age groups, even among children without comorbid ADHD, suggesting that this reduction is a component of the changing neurovegetative profile during adolescence rather than a by-product of decreased rates of comorbid ADHD in adolescents.

However, whereas we found that somatic complaints were present in 30%–50% of our sample (average 37% across all age groups), we did not find any age trends in the rate of somatic complaints in this sample. Notably, this lack of age effects was not due to age differences in comorbid anxiety disorders. Therefore, somatic complaints appear to be a common symptom in both depressed children and



adolescents; overall, it was reported at a higher rate than 4 depression symptoms, namely, weight loss, weight gain, hypersomnia, and guilt. Thus, somatic complaints should be considered an associated feature of the symptom profile of MDD in pediatric populations.

In regard to sex differences, while controlling for age effects and symptom intercorrelation, we found that girls had significantly higher rates of anhedonia, insomnia, and hypersomnia and lower rates of psychomotor agitation. This suggests that girls tend to have a more affective (anhedonia) and atypical (hypersomnia) presentation of depression across all developmental periods. Previous studies have yielded inconsistent results with regard to sex differences and depression symptoms. For example, 2 studies found higher rates of eating-related symptoms (eg, weight gain and increased appetite) among girls compared to boys,^{3,12} but this finding was not replicated in other studies,^{2,4,11} albeit with smaller samples. Such discrepancies may be partially due to methodological differences between earlier and current studies. For example, Williamson et al¹² reported sex comparisons only on symptoms of atypical depression and did not include all symptoms we assessed (eg, anhedonia, insomnia). Furthermore, the previous large sample studies used patients diagnosed during the normal course of clinical admission at a large psychiatric hospital. Our study was instead conducted with a clinical research sample that underwent a more comprehensive and controlled assessment process (eg, duplicate psychiatric interviews, best-estimate consensus diagnoses). It is possible that this resulted in more reliable diagnoses in our sample and less heterogeneity in comorbid symptoms and diagnoses, which could otherwise mask some of the sex effects we detected. Finally, it is also possible that the sex effects we observed may be more specific to psychiatric samples of European youth.

Finally, we were surprised that we failed to find any age-by-sex interaction in symptom rates. Given our large sample and analytic technique, we are confident that we would have been able to identify subtle interaction effects had they been there. This nonfinding is noteworthy, given that sex differences in the rate of depression diagnoses emerge during adolescence and that these sex differences have been related to cognitive, social, and physiologic developmental changes.¹⁰ However, our findings indicate that in clinically referred and psychiatrically-diagnosed depressed children and adolescents, sex differences in the symptomatology of depression are stable across developmental periods.

Limitations

Study participants were selected for a genetic study of risk factors of childhood-onset depression, and our sample selection was biased toward families with 2 or more children. In this article, however, we only included 1 child from each family. A further limitation is that depressive symptoms were examined as present or absent. This approach could have obscured more nuanced age and sex effects regarding

the severity (rather than rate) of specific symptoms. Finally, our sample encompassed different sex distributions across age groups. In younger ages, we had significantly more boys than girls, while in older ages we had significantly more girls than boys. Although our ALR model adjusts for such age and sex differences simultaneously, we still have an imbalance in sex ratios at the youngest and oldest age groups. This could limit our power to detect subtle sex differences specific to those age periods.

In conclusion, using a large clinical sample of depressed children and adolescents from Hungary, we observed significant developmental differences in the presentation of depression. Specifically, we noted an increase in vegetative symptoms with age. We also observed stable and elevated rates of irritability, which were concurrent with stable and low rates of anhedonia across all age groups. While current *DSM-IV* criteria indicate that irritability may be a substitute for depressed mood as a required symptom, our findings indicate that anhedonia, not depressed mood, is the infrequent symptom in this age group. Therefore, irritability should also be considered a substitute for anhedonia in this population. Our findings also suggest significant sex differences in the presentation of depression, but these differences are stable across development. Finally, our results replicate and extend prior findings with a similar large, US-based clinical sample,³ underscoring the transcultural similarity of MDD presentation in youngsters.

Author affiliations: Vadaskert Hospital, Budapest, Hungary (Drs Baji and Gáboros); the University of Pittsburgh School of Medicine, Department of Psychiatry, Pittsburgh, Pennsylvania (Drs Lopez-Duran, Kovacs, and Mr George); the Department of Child and Adolescent Psychiatry, University of Szeged, Hungary (Drs Baji, Mayer, Kapornai, Kiss, and Vetró).

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