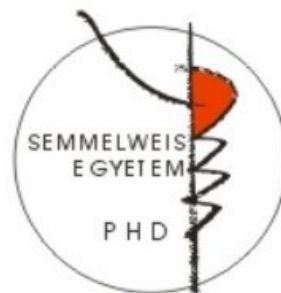


# Relationship of Childhood Onset Depression and Stressful Life Events in a Population-Based and Clinical Sample

Ph.D. theses

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## **I. INTRODUCTION**

Depression is the best known and the most common of all psychiatric diseases, and will, according to WHO, constitute an even more significant health problem and economic burden worldwide in the next few decades. Depressive symptoms (and the depressive disorder) is becoming more and more frequent in childhood and mainly in adolescence; the lifetime prevalence of adolescent depression is nearly equal to those of adulthood depression. Adolescent girls are especially at risk..

Numerous depressive symptoms, if they exist for a long time, diminish the child's adaptive capacity, school-performance, behavior and quality of life. We need to emphasize the association between childhood depression and suicide. In spite of the significance of depression, only few Hungarian studies are published about the prevalence of childhood depression and its risk factors.

Many international studies suggest that besides genetic and biological factors, psychosocial and environmental factors also play an important role in the onset of depression. We would like to emphasize the importance of considering stressful life events among the psychosocial risk factors, besides socio-economic and socio-demographic characteristics. Among sociodemographic characteristics, age and sex have a key influence on the frequency of symptoms.

The relationship between life events and depression has been the subject of extensive psychiatric research in the last 30 years. Studies mainly focused on the association between adulthood depression and stressful life events. Research of "distal" events as risk factors of adulthood depression and the association of life events with the first depressive episode inspired the investigation of life events with respect to childhood depression. Examinations of clinical and community samples collected mainly from adolescents showed an association between the total number of experienced life events, life event groups, specific life events, and depression. Some studies called attention to the fact that the accumulation of life events increases the risk of depression. Only few studies focused on the relationship between life events and depression in children of a younger age group; data on the relationship between stressful life events and depression in pediatric clinical populations are more limited. At the same time, it can be stated, that the examination of the relationship between childhood onset depression and the life events is very diverse; authors use many different approaches in their studies.

One part of the community-based and clinical studies examine the prevalence of life events (and life event groups) and the gender differences in the experience of life events. A wide variety of events, such as parents' separation or divorce, exposure to family conflict, teasing, moving, abuse, parental death and parental depression have all been related to children's depressive symptoms or childhood-onset depression. However, previous studies have usually focused on a single life event, but we have only very limited data available concerning possible interactions between age and gender.

## **II. AIMS**

Our aim was to examine the association between stressful life events and childhood onset depression on community and clinical samples. In the first step we examined the depressive symptoms and stressful life events, in the second phase, we considered the relationship between childhood onset major depression and stressful life events.

In our community-based study we analyzed the frequency, the severity, the age and gender differences of childhood and adolescent depressive symptoms. We wanted to determine the frequency of stressful life events among 7-15 year old students. We assumed, that the experience of more life events increases the risk of depressive symptoms. We also hypothesized that certain stressful life events have different effects on the symptoms of childhood onset depression. Our aim has been to prove that there are certain stressful life events that play a more decisive role in the development of the symptoms of childhood depression than others, with regards to both frequency and characteristics.

In our clinical study we examined children with major depression compared to the normative sample. We hypothesized that children in the depressive sample have stressful life events more frequently than in the normative sample. We assumed that the depressed children are distinguished by having experienced certain kinds of life events. We hypothesized that the number of life events varies by age and sex differently in depressed vs. normative children, and that depressed children are distinguished by a characteristic pattern of life events, the effect of which is moderated by age and sex.

The present study investigates the association of life events and childhood depression in an age-group (7-12 years) that, to our knowledge, has not been examined so far. The large sample size in our study enables us to analyse gender and age interactions.

### **III. COMMUNITY-BASED STUDY**

#### **III.1. METHODS**

##### **III.1.1.PARTICIPANTS**

For the community sample we collected data in 9 elementary schools in two regions of Hungary. First, we sent out 5224 questionnaires to parents. Second, through the schools, self-reported questionnaires were given to those children whose parents had previously given their consent by returning the packet of completed consent forms to the school. As with the parents, participation of children was also voluntary. We received completed questionnaires from 67.4% of the parents. In this study we only examined results from forms fully completed both by students and their respective parents (N=2652). Age range of the respondents was between 7 and 15 years. Gender distribution was 44.6% boys and 55.4% girls. Mean age was 10.45 years.

##### **III.1.2. MEASUREMENT**

###### **III.1.2.1. DEPRESSIVE SYMPTOMS**

Depressive symptoms were measured by the short version of Child Depression Inventory (CDI), which originally contains 27 items. The short form version (CDI-S) contains 10 items with 3 response choices for each item, each choice coded as 0, 1, or 2 respectively. Thus, the maximum of the depression scale is 20 points. In the short version of CDI a cut-off score is 7 points. In our research, based on the examination material of children with major depression we determined the lower cut-off score as 5. Thus, in our population-based study, 5 points or more have indicated an increased risk of depression, while those who have score 7 points or more have been considered as suffering from clinical depression.

###### **III.1.2.2. STRESSFUL LIFE EVENTS**

Stressful life events were collected from the parents through the self-report version of the Intake General Information Sheet (IGIS), a fully structured questionnaire for parents that contains different sociodemographic and socioeconomic parameters of the child and their family. The questionnaire covers the familial conditions, developmental, physical health, school achievement, peer relations, and the main life-events relevant to the child. We asked parents to report whether their child had ever experienced a specified life-event, or not. We analysed 26 stressful life events, which, according to the

literature, could have influenced childhood mood and behavior.(e.g.: death of a close relative, illness of parents, divorce of parents, abuse of children).

### III.1.3. STATISTICAL ANALYSES

The data analysis was conducted with SPSS 13.0 for Windows. Statistical tests like Frequencies, Chi-Square, Two Independent Samples T-Test presenting the differences between age and gender. Exploring the relationship between the same variables we took Bivariate Correlation (Linear) and counted Pearson Correlation Coefficients. The Linear Regression Model helped to show the indicators in terms of depression. Multi-linear Regression was used with the dependent variable Level of Depression. We ran Logistic Regression – Odds Ratios with Confidence Interval 95% to analyze what kind of risk factors are there with exact life events related to the appearance of depression symptoms.

### III.2. RESULTS

The mean depressive score on the CDI was 3.61. Boys obtained 3.44 points (SD=2.72); girls got 3.76 points (SD=2.88), on average, although the mean depressive score of 7-8 year-old boys was higher than that of the girls. From the age of 9, the mean depressive score of boys did not show a significant change, while that of the girls increased with age. 14.9% of the students (boys 12.7%, girls 16.6%) had a score of 7 or more that implies an increased risk of clinical depression.

Among the 26 stressful life events examined children experienced  $2.35 \pm 1.87$  on average. We found significant positive correlation between depressive symptoms and stressful life events. The prominence of the relationship between the two variables was not significantly influenced by the age and sex of the child. We can conclude already on the basis of our population-based experiments that life events in childhood and adolescence have an effect on depressive symptoms. The larger the number of life events experienced by the child, the larger the risk of developing depressive symptoms.

Among the 26 specific life events examined we have found that divorce, regular familial arguments, and teasing have showed the strongest relationship with depressive symptoms In boys four life events (serious somatic and mental illness of father, family argument, and teasing), in girls six events (divorce of parents, family argument, psychiatric illness of sibling, financial problems, moving and teasing) caused a 1.5-5.5-fold increase in the risk of the development of depressive symptoms in children.

The accumulation of certain specific life events further increased the risk of depressive symptoms. When children experienced all three of important life events (parental divorce, familial argument, and peer teasing) the risk of depression was almost 5 times higher.

#### **IV. CLINICAL STUDY**

##### **IV.1. METHODS**

###### **IV.1.1. PARTICIPANTS**

Children were recruited through 23 child psychiatric facilities across Hungary. Inclusion criteria were the following: 7.0 years to 14.9 years old, not mentally retarded, no evidence of major systemic medical disorder, had available at least one biological parent and one sibling (specified by the study's genetic component), and attained a predetermined cut-off score on one of various symptom scales.

The clinical sample consisted of 434 children with MDD, the mean age was 11.6 year. To be included, children had to be 7.0 years to 14.9 years old. The group is constituted by those children who were selected to participate in the research investigating the risk factors of depression. The parental informant was the biological mother, and during the first interview the child was experiencing his or her first depressive episode.

The normative sample consisted of 724 community children (399 girls) mean age was  $10.8 \pm 2.2$  year. The normative group was selected from among children who had participated in a population-based research conducted in two regions of the country. We considered those students – similar to the depressive group – who had a sibling, and whose parental informant was the biological mother. Subjects with mental retardation or any major systemic medical disorders were excluded.

The depressed group had proportionally more boys (54.1% versus 44.9%) and was, on average, older  $11.6 \pm 2.0$  years versus  $10.08 \pm 2.2$  years than the normative group.

###### **IV.1.2. MEASUREMENT**

###### **IV.1.2.1. MAJOR DEPRESSIVE DISORDER**

We used ISCA-D (Interview Schedule for Children and Adolescents - Diagnostic Version) semi-structured clinical diagnostic interview to establish the diagnosis of major childhood depression. Children meeting these criteria were scheduled for a 2-part evaluation, conducted on 2 separate occasions, about 6 weeks apart, by different

clinicians. We obtained written consent for participation signed by both parents and the child.

#### IV.1.2.2. STRESSFUL LIFE EVENTS

To examine the 26 stressful life events, we used the IGIS. We asked parents to report whether their child had ever experienced a specified life-event, and we analyzed the data of those children whose informant was the biological mother. In the depressed group we used the interview-form, in the normative group the self-reported form.

We did not only examine the 26 life events one by one, but we established 4 clinically significant life event clusters (parental health, death, intrafamilial- and socioeconomic life events). Four specific life events did not fit into these clusters, consequently, these constituted a so called miscellaneous cluster (abuse, teasing, police contact, suspension from school).

#### IV.1.3. STATISTICAL ANALYSES

The data analysis was conducted with SPSS 13.0 for Windows. Statistical tests like Frequencies, ANOVA, Two Independent Samples T-Test presenting the differences between age and gender. Exploring the relationship between the same variables we took Bivariate Correlation (Linear) and counted Pearson Correlation Coefficients. We ran Logistic Regression – Odds Ratios with Confidence Interval 95% to analyze what kind of risk factors are there with exact life events related to the appearance of major depression.

Describing the life events in the depressed group multivariate analysis was applied. We ran Hierarchical Logistic Regression – Stepwise selection of life events with Confidence Interval 95% because we intended more thorough analysis with the interactions of age and gender.

#### IV.2. RESULTS

We examined the relationship between life events and major depression among children and adolescents in three of several ways (namely, through the examination of the total number of life events, clusters of life events, specific life events).

The depressed sample endorsed far more life events ( $6.0 \pm 2.8$ ), twice as many as the normative sample ( $2.8 \pm 2.0$ ). The number of total life events did not differ by sex in either group. Age was not correlated with life events in the depressive sample, but a weak but significant positive correlation was observed in the normative sample. This suggests that older children in the normative sample had more life events (mean of

almost 4 in 15-year-olds versus 2.4 in 7 year olds), but still far less than in any age group in the MDD sample. At each age in the depressed sample, an average of 5.5 – 6.5 stressful life events were reported.

Each event queried was endorsed significantly more frequently in the depressed group than the normative group with the exception of very rare events (i.e., physical and mental illness of stepparents, foster care, and suspension from school). A further examination of the relationship between major depression and specific life events and life event groups a characteristic life event pattern became discernible.

Notwithstanding age, three event clusters increased the odds of being in the depressed group: “parental health” doubled and “intrafamilial events” nearly tripled the odds. Death events increased the odds in younger children nearly 5 fold, but this effect was attenuated in older children.

Within the “miscellaneous events” cluster, three specific events have been found to increase depression, regardless of age and sex: history of abuse (OR = 8.5), teasing (OR = 12.9), or police contact (OR =13.5).

Three further life events were significantly associated with the depressed sample regardless of age and gender: medical hospitalization of father (OR=1.66), medical hospitalization of sibling (OR=1.70), and psychiatric hospitalization of the mother (OR=3.06). Five events interacted with age: the experience of a natural disaster, maternal somatic illness, psychiatric hospitalization of the father, death of a relative, parent unemployment. In the first four cases, the odds of depression were increased in children under 11, while the significant relationship with depression decreased with age. In its turn, parental unemployment constitutes a risk factor largely in older children. Two events interacted with age and gender, divorce and family arguments. In girls under 9, divorce increased the risk of depression 5-10 fold, while in older girls, this risk decreased significantly (change in OR = 0.74 per year). In boys, the approximately two-fold odds ratio showed only a slight decrease with age. In a similar fashion, exposure to family arguments was a significant predictor of depression in younger boys (OR = 2.09), with a slight decrease in an older age (change in OR = 0.91 per year). However, exposure to family argument became a more significant risk factor in girls as they grew older (OR= 2 in age 10, OR = 5-6 in ages 15-16).

## **V. CONCLUSIONS**



The strength of our research is that it analyses the prevalence in Hungary of depressive symptoms on a large population sample. Furthermore, our research is unique since it examines the stressful life events and their association with childhood and adolescent onset depression in a so far not considered early age, in a large-size clinical-, normative - and population sample. Our study emphasizes those specific life events, which can particularly increase the risk of depressive symptoms and major depressive disorder in the respective sexes..

It could be equally important for teachers, school mental health workers, and for parents...to have a knowledge of the prevalence of depressive symptoms. Experts, who work on preventive programs should keep in mind the fact that one third of primary school children have more than one depressive symptom, and 15% of them probably have depressive disorders. Boys aged 7-10 and girls aged 13-14 are especially at risk; every fifth girl of this age group can suffer from depressive disorder.

In our present study we could analyze the association between stressful life events and childhood onset depression in both population-based and clinical samples. Our finding that depressed children experience a lot more life events than their non-depressed peers do corresponds to the results of international studies. One of the most important findings is that rapidly and early on (i.e. by ages 7 to 9) accumulated stressful life events can launch the onset of depressive disorder. The age interactions call attention to the significance of the life events of the first 10 years, as the risk factors of childhood depression.

Practical considerations make the role of certain specific life events more important. . The life event pattern that became discernible in the population sample, partially corresponded with the life event pattern of the depressed sample. In the latter case, the pattern was certainly more pronounced and it was characteristic of both sexes and different ages.

Thus we can conclude, that depressed children can be identified promptly with the simple questionnaire that we used in the population sample, and that specific life event pattern of the depressed children can also be defined. These life events occur very often and are easy to recognize in everyday practice. If child care professionals keep in mind that the frequently occurring and easily recognizable stressful life events may cause depression, they will be able to contribute to the early detection of depressive

symptoms, and they can solicit help in a timely fashion after the onset of the disease. The knowledge of life events as risk factors of depression can help clinicians to plan the process of the therapy. To know the age and sex differences can be helpful in working on special preventive programs. Early detection and treatment can be achieved through the effective cooperation of school personnel, mental health workers, and clinical experts.

## **PUBLICATIONS RELEVANT TO THE DISSERTATION**

Mayer L, Kiss E, Baji I, Skultéti D, Vetró Á. (2005) Relationship of demographic characteristics and psychopathological risk factors in a school-age population. *Fejlesztő Pedagógia*, 5-6: 36-40.

Mayer L, Kiss E, Baji I, Skultéti D, Vetró Á. (2006) Relationship of depressive symptoms and life events in a school-age population. *Psychiatr Hung*, 3: 210-218.

Mayer L, Kiss E, Baji I, Skultéti D, Vetró Á. (2006) Quality analysis of life events and their relationship to depressive symptoms in a school age population. *Psychiatr Hung*, 5: 360-370.

Mayer L, Lopez-Duran NL, George C, Baji I, Kapornai K, Kiss E, Kovacs M, Vetró Á. Characteristics of stressful life events in a clinical sample of depressed children in Hungary. *J Affect Disord* (közlére elfogadva).

Kiss E, Baji I, Mayer L, Skultéti D, Benák I, Vetró Á. (2007) Validity and psychometric properties of a quality of life questionnaire in a Hungarian child and adolescent population. *Psychiatr Hung* 1:33-42.

Kapornai K, Gentsler AL, Tepper P, Kiss E, Mayer L, Tamás Zs, Kovacs M, Vetró Á. (2007) Early development and features of Major depressive Disorder in a child clinical sample in Hungary. *J Affect Disord*, 100: 91-101.

Liu X, Buysse DJ, Gentzler AL, Kiss E, Mayer L, Kapornai K, Vetró Á, Kovacs M. (2007) Insomnia and Hypersomnia Associated with Depressive Phenomenology and Comorbidity in Childhood Depression. *Sleep*, 30: 83-90.

Feng Y, Wigg K, King N, Vetró Á, Kiss E, Kapornai K, Mayer L, Gádoros J, Kennedy JL, Kovacs M, Barr CL (2007) GPR50 is not Associated with Childhood-Onset Mood Disorders in a Large Sample of Hungarian Families. *Psychiatric Gen*, 17: 347-350.

Dempster E, Kiss E, Kapornai K, Daróczy G, Mayer L, Baji I, Tamas Z, Gadoros J, Kennedy JL, Vetró Á, Kovacs M, Barr CL. (2007) No evidence of association between a functional polymorphism in the MTHFR gene and childhood-onset mood disorders. *Mol Psychiatry*, 12: 1063-1064.

Feng Y, Vetró Á, Kiss E, Kapornai K, Daróczy G, Mayer L, Tamás Zs, Baji I, Gádoros J, King N, Kennedy JL, Wigg K, Kovacs M, Barr CL. (2008) Association of the Neurotrophic Tyrosine Kinase Receptor 3 (*NTRK3*) Gene and Childhood-Onset Mood Disorders. *Am J Psychiatry*, 165: 610-6.