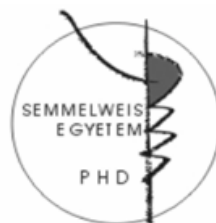


Examining Child Psychiatric Disorders:
Special Focus on ADHD and the Quality of Life

Doctorial theses

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1. Introduction

1.1 *Quality of Life (QoL)*

The concept of Quality of Life (QoL) of patients with mental health disorders gained increasing importance in the last decades. Although assessing the functional status of the patients had been important previously, only functional impairment is required for diagnosis. The concept QoL is much broader.

The definitions of QoL include the somatic, social and psychological areas. Rating QoL, subjective aspects come ahead, however recent studies highlighted, that a proxy,, “objective report” is also needed. In case of surveying the QoL of children, it is acutely important, that we cannot solely rely on the self-report judgment of the children. A proxy report - who used to be one of the parents in our study - is also needed. It might be interesting, how much the child’s and the parent’s reports are the same.

1.2 *Attention Deficit / Hyperactivity Disorder (ADHD)*

One of the main psychological disorders appearing in childhood and puberty is ADHD, which stays during adulthood in 30-60% of the cases. Its symptoms affect mobility, attention efficacy and also impulsivity. ADHD often comes with comorbid disorders, which have a main impact on both diagnostic and therapeutic progress. Comorbid disorders are more frequent with higher age.

1.3 *ADHD and the QoL*

Due to the symptoms of ADHD several problems come up during everyday life: they affect the performance in school and also the relations with parents and peers. ADHD affects many areas of child development, so its impact on QoL seems to be an important question. Previous findings indicate controversial results regarding the effect of age and gender on QoL of children with ADHD.

1.4 *Categorical and dimensional approach of disorders, subthreshold ADHD*

The classifications systems based on categorical approach determine the criteria when a diagnosis (for example the diagnosis of ADHD) can be set up. However, in the last decade in psychiatry the mental health disorder’s dimensional approach came ahead. The subthreshold disorders – which are also based on categorical approach, but do not require

all criteria of the classification systems - offer a conjunctive solution between categorical and dimensional theses. Many researches call attention to the fact, that also subthreshold disorders might cause functional impairment. Although subthreshold ADHD is not examined enough, it has gained more and more attention in the last years.

2. *Objective of the study*

The objective of my doctoral dissertation was to examine the dimensional approach of psychiatric disorders and QoL on clinical sample.

In the first part of my work, I examined the following questions with children who were referred for psychiatric assessment for the first time:

1. Do the subthreshold symptoms of the main psychiatric disorders lead a child who does not fulfill any psychiatric diagnosis to get psychiatric assessment? If yes, which disorder's symptoms increase the possibility that a child, who does not fulfill any psychiatric diagnosis, gets psychiatric assessment?
2. Does the decrease of QoL lead a child, who does not fulfill any psychiatric diagnosis, to a psychiatric assessment? If yes, in what extent?

Our first findings suggest that both the subthreshold symptoms of ADHD and the decreased QoL are factors that might increase the possibility to lead a child who does not fulfill any psychiatric diagnosis to psychiatric assessment (see later). These findings raise the question what kind of a relation exists between ADHD and QoL and which factors affect this correlation. Furthermore, our aim was to provide further empirical data to the debate, whether the child or an outsider (in our case, a parent) is the most efficient by rating QoL.

In the second part of my doctoral dissertation my aim was to examine the following questions on a sample of children/adolescents with ADHD who got into the supply system for the first time.

1. What kind of relations do we find between ADHD and QoL? How do the following factors: age, gender, type of ADHD, comorbid disorders affect the relation?
2. What kind of an effect the above mentioned factors have on the QoL rated by the child and by the parent?

3. Methods

3.1 Participants

The study was approved by the Scientific Research Ethics Committee of the Ministry of Human Resources.

We tried to enrol all new cases into the study in the Vadaskert Child Psychiatric Hospital and Outpatient Clinic during the recruitment period of 04.09.2006 and 30.11.2011. The control group was recruited from the local, normal population, using convenience sampling.

Inclusion criterion was age below 18, no minimum age was determined. Exclusion criterion was mental retardation in the medical history. Inclusion criterion regarding the control sample was that the child was not under psychiatric or psychological treatment.

3.2 Measures

We measured psychiatric symptoms and diagnoses with the adapted, Hungarian version of Mini International Neuropsychiatric Interview Kid (MINI Kid). MINI Kid is a short, comprehensive, structured diagnostic questionnaire.

To assess QoL we applied the Hungarian version of the *Inventar zur Erfassung der Lebensqualität bei Kindern und Jugendlichen* (ILK Scale). We used both the child and the parent versions, which are validated general QoL assessing questionnaires.

The parents/tutelaries also filled in a simple demographic data sheet regarding the children (gender, age, perinatal anamnesis, type of school, siblings, parents' age, parents' educational attainment, parents' job, if they live together, family anamnesis).

3.3 Statistics

Besides descriptive statistics, χ^2 -test, t-tests, Mann-Whitney test and Kruskal-Wallis test were used to assist the relationship between the test groups. Furthermore, we used Spearman's correlation coefficient to evaluate bivariate relationships.

In the first section, logistic regression analysis with forward stepwise selection was computed to analyse the effects of the number of symptoms reported in the MINI Kid diagnostic sections of the psychiatric referral of a child or adolescent without MINI Kid diagnosis. In the second analysis, hierarchical multiple regression analyses (MRAs) were used to assess the relationships between measures of QoL, demographics, characteristics of ADHD, and comorbid psychopathology reported in the MINI Kid.

Data were analyzed using IBM SPSS Statistics 20 (SPSS Inc. 2011). An α -level of .05 was considered to be significant. Bonferroni correction was applied to control for multiple comparisons.

4. Results

4.1. Participants

The clinical group consisted of 418 children (mean age=10.82, SD=3.81), and the control group consisted of 48 children (mean age=10.38, SD=3.77). The clinical group consisted of 294 boys (70.3%) and 124 girls (29.7%), while the control group consisted of 19 boys (39.6%) and 29 girls (60.4%). The groups showed significant difference regarding gender ($\chi^2 = 18.46$, $df=1$, $p < 0.001$). Regarding age, there was no significant difference ($t = -0.76$, $df=464$, $p = 0.447$).

The secondary analysis focused on the children with ADHD diagnosis regarding MINI Kid (N=211). After excluding cases because of missing data, 178 (84.3%) parent-child dyads were included in the analysis, there were 148 boys (83.1%), mean age was 9.33 years (SD=3.30). The group of boys were significantly younger than the group of girls ($M_{boys} = 8.90$, $SD_{boys} = 3.10$, $M_{girls} = 11.43$, $SD_{girls} = 3.47$, $t = 3.998$, $df = 176$, $p < .001$).

4.2 First study

Among children from the clinical group included in the analysis 61 children had no MINI Kid diagnosis. There were 19 girls and 42 boys (mean age=10.77, SD=3.85) in this subgroup, while in the other subgroup (children how had one or more diagnosis according to MINI Kid) there were 105 girls and 252 boys (mean age=10.82, SD=3.81). Among the three subgroups (children without MINI Kid diagnosis, children with one or more MINI Kid diagnosis, and the control group) we found no difference in age (Kruskal-Wallis test: $H(2, N=466) = 0.627$, $p = 0.731$) but significant gender differences ($\chi^2 = 28621.0$, $df = 465$, $p < .001$).

Comparing the referral (clinical) and the control groups, children who were referred for psychiatric assessment reported significantly more symptoms than controls in the MINI Kid ($M = 42.77$, $SD = 22.01$ and $M = 18.69$, $SD = 16.57$, and $t = -9.182$, $df = 464$, $p < .001$). Children who were referred for psychiatric assessment with MINI Kid diagnoses

reported significantly more symptoms in the MINI Kid compared with controls ($z = 8.755$, $p < .001$) and with children who were referred for psychiatric assessment without MINI Kid diagnoses ($z = 9.697$, $p < .001$). However, no differences were found between the control group and the referred subgroup without MINI Kid diagnoses ($z = 0.012$, $p = 1.000$).

Comparing the referral and the control groups, children who were referred for psychiatric assessment reported significantly more impairments in QoL than the control group ($M = 16.14$, $SD = 4.46$ and $M = 12.85$, $SD = 3.43$, respectively, $t = -5.887$, $df = 385$, $p < .001$). Among the three study groups (referred subgroup without MINI Kid diagnosis, referred subgroup with one or more MINI Kid diagnoses, and the control group), significant differences were found regarding self-related QoL ($H(2, N = 394) = 27.126$, $p < .001$). Specifically, the control group showed significantly less impairment when compared with both referred subgroups without ($z = 2.457$, $p = 0.042$) and with – one or more – MINI Kid diagnoses ($z = 5.129$, $p < .001$); the two referred subgroups did not show significant differences in the level of impairment in QoL ($z = 1.410$, $p = 0.479$).

In the multivariate analysis of the effect of the number of symptoms reported in all MINI Kid diagnostic sections on group membership (1. referred subgroup without MINI Kid diagnosis or 2. control group) our model suggested that boys were more often referred for psychiatric assessment than girls, whereas age did not have a significant effect.

After controlling for other variables in the model, results showed that the odds of referral for psychiatric assessment increased 16% with every one additional ADHD symptom and decreased from 1.0 to .535 with every additional social phobia symptom.

4.3. Second study

Regarding gender, boys rated QoL significantly higher than girls ($M_{\text{boys}} = 19.38$, $SD_{\text{boys}} = 4.88$, $M_{\text{girls}} = 25.03$, $SD_{\text{girls}} = 6.55$, $t = 4.476$, $df = 176$, $p < 0.001$), however we found no significant difference regarding gender between QoL rated by the parents ($M_{\text{boys}} = 22.09$, $SD_{\text{boys}} = 4.19$, $M_{\text{girls}} = 23.47$, $SD_{\text{girls}} = 3.86$, $t = 1.658$, $df = 176$, $p = 0.099$).

Analysing the effects of child's age and gender on QoL measures, we have got the following result: in the first step of the MRAs, child's age and gender were entered into the regression analysis to be able to control for these variables. Using self-report ILK scores as dependents, both child's age ($\beta = .291$, $p < 0.001$) and gender ($\beta = -.295$, $p < .001$) demonstrated significant effects on the self-reported QoL scores, accounting for 22.1% of the variance, $F(2, 175) = 24.827$, $p < .001$.

Lower self-reported QoL was associated with female gender and higher age. We found significant positive correlations between child's age and parent report ($\beta = 0.210$, $p = 0.007$, $\Delta R^2 = 0.056$, $F(2,175) = 5.197$, $p = 0.006$).

Analysing the effect of ADHD subtypes and comorbid diagnoses on QoL measures we have got the following result: using the categorical approach, at Step 2 of the MRA, the effects of subtypes of ADHD were non-significant for all dependent variables. In the third and final step, the six comorbid diagnostic groups (0 = no diagnosis; 1 = at least one diagnosis) were added to the regression equations using the stepwise method. When using self-report ILK scores as dependents, the forward stepwise procedure added trauma-related disorders firstly ($\Delta R^2 = 0.028$, $\beta = 0.177$, $p = 0.012$), and ODD/CD secondly ($\Delta R^2 = 0.018$, $\beta = 0.136$, $p = 0.044$), indicating that these comorbid diagnoses are related to lower self-reported QoL.

For parent-reported QoL as a dependent, the forward stepwise procedure added three variables: any diagnosis of anxiety disorders firstly ($\Delta R^2 = 0.063$, $\beta = 0.258$, $p < .001$), MDE/dysthymia secondly ($\Delta R^2 = 0.035$, $\beta = 0.207$, $p = 0.008$), and ODD/CD third ($\Delta R^2 = 0.025$, $\beta = 0.161$, $p = 0.023$), indicating that these comorbid diagnoses are related to lower parent-reported QoL.

We also analysed the effects of symptoms of ADHD and comorbid conditions on QoL. When exploring our hypotheses in a dimensional approach, in the second step of the MRAs, the number of symptoms of attention deficit, as well as hyperactivity/impulsivity, was entered, but these variables yielded a non significant contribution to the models for all dependent variables. At the third step, the number of symptoms in each of the six comorbid diagnostic groups was added using the stepwise procedure. When using self-report ILK scores as dependents, firstly the number of anxiety symptoms ($\beta = .298$, $p < .001$) were added, accounting for a further 6.8% of the variance, and secondly the number of symptoms (PTSD/adjustment disorder) of trauma-related disorders ($\Delta R^2 = .020$, $\beta = .156$, $p = .025$), indicating that more symptoms of these comorbid conditions are associated with lower self-reported QoL.

For a parent-reported QoL as a dependent, the forward stepwise procedure added two variables: firstly the number of symptoms of MDE/dysthymia ($\beta = 0.432$, $p < .001$), accounting for an additional 8.6% of variance and secondly the number of symptoms of anxiety disorders ($\Delta R^2 = 0.028$, $\beta = 0.206$, $p = 0.016$). These results indicate that the increasing numbers of these comorbid conditions are related to lower parent-reported QoL.

5. Conclusions

My doctoral dissertation's central thread consist of two elements, the dimensional approach of psychiatric disorders and QoL which are not, or vaguely represented in current classification systems, however recent researches' results suggest their importance.

Furthermore, in my research I analysed ADHD symptoms as found results in the first study and deliberately selected sample in the second study. My doctoral dissertation consists of a clinical and a control group processed in two phases. Below, I am going to discuss the main results of this examination in detail from more angles.

5.1. First study

Research of my doctoral dissertation – which is the first of its kind to our knowledge – analyses the role of the subthreshold disorders and QoL in the process of children psychiatric evaluation.

Remarkable result, that almost every sixth child, who goes under psychiatric evaluation did not fulfill the classification system's diagnostic criteria according to a structured diagnostic questionnaire.

Furthermore, among the children of the control group – in whose medical history there was no current or past psychiatric/ psychological treatment – more than one third was diagnosed with at least one psychiatric disorder according to the structured diagnostic questionnaire.

In summary of the first study of my doctoral dissertation, it can be stated, that decreased QoL and ADHD symptoms are risk factors for psychiatric evaluation, even in case of subthreshold psychiatric abnormalities (thus the current diagnostic criteria are not met). The symptoms of social phobia could act as protecting factors reducing the possibility of a psychiatric evaluation, although these children are not getting the professional help they needed. If psychiatric evaluation is the way to get the professional help, the ADHD can act as protecting factor while the social phobia is the risk factor.

Based on our results, we have to outline that recognizing and evaluating the subthreshold psychiatric disorders, the subthreshold ADHD, social phobia and the QoL have key importance in secondary prevention.

Secondary study

The second study of my doctoral dissertation is the very first which – using a large sample - takes both dimensional and categorical approaches into consideration while examining QoL of children not have been diagnosed with ADHD earlier.

According to the results of the second study of my doctoral dissertation, I would like to highlight, that age, gender, and comorbid disorders (for example: ODD/CD, trauma related symptoms, mood- and anxiety disorders) are key factors in rating QoL of children with ADHD not have been treated before.

The results of our analysis prove the past findings that both dimensional and categorical approaches have to be used.

Furthermore, based on my doctoral dissertation's results, to take into consideration both the self- and parent rated QoL in case of children with symptoms of ADHD is also important in clinical practice and research.

5.2 Limitations of my dissertation

- 1) The control group was recruited from the local community through word of mouth.
- 2) There were significant gender differences between the referred group and the control group.
- 3) Due to the cross-sectional study design, associations do not indicate causality, longitudinal studies are needed to understand the causality.
- 4) Although all interviewers participated in a training course before the study and were regularly supervised, we did not measure inter-rater reliability.
- 5) Although the M.I.N.I. Kid provides a wide variety of DSM-IV child/adolescent psychiatric disorders, it does not assess all possible psychiatric disorders, i.e. learning disorders.
- 6) Other variables can be among the reasons of referral for psychiatric assessment as well, such as the family condition or socioeconomic status, however, this survey did not measure these aspects.
- 7) As we examined treatment naïve children with ADHD, we can assume that older children, who were referred for treatment for the first time at this age, belonged to the less severe end of the spectrum.
- 8) Similarly to all clinical researches, the prevalence of boys with ADHD was higher, so our survey is less informative about girls.
- 9) Although mental retardation was an excluding criterion, the information about it was

based on the medical history.

- 10) Parental psychopathology was not measured; however it might affect the parent's rating.
- 11) Although we measured more demographic factors, we did not include social economical status, which also might affect the QoL.
- 12) It would have been useful to apply rating scales as well when measuring psychiatric disorders.
- 13) Missing data was more frequent in older and less severe cases.

6. New results of my doctoral dissertation

- 1.) I am the first one, who analyzed the effects of QoL and subthreshold disorders in case of children who were referred for psychiatric evaluation but did not fulfill any psychiatric diagnosis. Decreased QoL and ADHD symptoms are risk factors for psychiatric evaluation, even if they remain subthreshold, while the symptoms of social phobia have an opposite effect.
- 2.) According to self-ratings of children with ADHD decreased QoL is related to female sex and higher age. In the light of dimensional approach it is related to the symptoms of anxiety and traumas, while according to categorical approach it is related to the disorders connecting to traumas, and to oppositional defiant disorder and behavioral disorder.
- 3.) According to parent ratings of children with ADHD decreased QoL is related to higher age. It is related to anxiety- and mood disorders according to dimensional approach, and to oppositional defiant disorder and behavioral disorder according to categorical approach.

7. List of own publications:

7.1 Publications connected to the topic of the dissertation:

Dallos Gy, Miklósi M, Keresztény A, Velő Sz, Szentiványi D, Gádoros J, Balázs J. Self- and Parent-Rated Quality of Life of a Treatment Naïve Sample of Children With ADHD: The Impact of Age, Gender, Type of ADHD, and Comorbid Psychiatric Conditions According to Both a Categorical and a Dimensional Approach. *Journal of Attention Disorders*. 2014 Jul 11. [Epub ahead of print]

DOI: 10.1177/1087054714542003

IF: 2.397

Dallos Gy, Keresztény A, Miklósi M, Gádoros J, Balázs J. (2014) Why are children and adolescents referred for psychiatric assessment without fulfilling diagnostic criteria for any psychiatric disorder? *Child and Adolescent Mental Health*. 19(3):199–207
DOI:10.1111/camh.12046

IF: 0.954

Velő Sz, Keresztény A, Miklósi M, **Dallos Gy**, Szentiványi D, Gádoros J, Balázs J. (2014) „Frissen” diagnosztizált, kezelést még nem kapó figyelemhiányos-hiperaktivitás zavarú gyermekek és serdülők életminősége. *Psychiatria Hungarica* 29(4):410-417

Dallos Gy, Balazs J. (2014) A figyelemhiányos-hiperaktivitás zavar hatása az életminőségre: esetbemutatók. *Neuropsychopharmacol Hung*. 16(2):91-97

Keresztény Á, **Dallos Gy**, Miklósi M, Róka A, Gádoros J, Balázs J. (2012) A gyermek- és serdülőkorú figyelemhiányos-hiperaktivitás zavar komorbiditásainak összehasonlítása. *Psychiat Hung*. 27(3):165-173

7.2 Other peer-reviewed publications:

Balázs J, Miklósi M, Keresztény A, **Dallos Gy**, Gádoros J. (2014) Attention-Deficit Hyperactivity Disorder and Suicidality in a Treatment Naïve Sample of Children and Adolescents. *J Affect Disor* 152-154:282-7. DOI: 10.1016/j.jad.2013.09.026

IF: 3.705

Balázs J, Vizi J, **Dallos Gy**, Ilku L. (2013) Jogi-etikai problémák a gyermekek gyógyszeres kezelésében – gyermekpszichiátriai példákon bemutatva. *IME, Egészség-gazdaságtan* 12:34-39

Balázs J, Tolna J, Gádoros J, **Dallos Gy**. (2012) Felnőttkor – gyermekkor – felnőttkor: Hosszútávú kezelés a gyermek és felnőtt pszichiátriában. *Neuropsychopharmacol Hung* 14(1): 51-58

Balázs J, **Dallos Gy**, Keresztény A, Czobor P, Gádoros J. (2011) Methylphenidate Treatment and Dyskinesia in Children with Attention-Deficit/Hyperactivity Disorder. *J Child and Adoles Psychopharm* 21(2):133-138

IF: 2.884

Balázs J, **Dallos Gy**, Németh L, Bíró A, Prekop Cs, Gádoros J. (2006) Gyermekpszichiátriai epidemiológia. *Orvostovábbképző Szemle (Suppl)*, Szept: 3-15

7.3 Abstracts that can be cited

Balázs J, **Dallos Gy**, Keresztény A, Gádoros J. (2011) Suicide behaviour and subthreshold psychiatric disorders among children and adolescents. *European Psychiatry* 26, Supplement 1: 265

Balázs J, **Dallos Gy**, Keresztény A, Gádoros J. (2010) Gender differences in adolescent suicide behaviour. *European Psychiatry*, Volume 25, Supplement 1, pp:1345

Balázs J, **Dallos Gy**, Gádoros J. (2009) Relationship between mental disorders and suicidal behavior among children and adolescents in a psychiatric department. *European Neuropsychopharmacology*. 19. (Suppl3): 680-680

Bálint M, Bartha Zs, Berger N, Burits A, **Dallos Gy**, Gábor R, Keresztény Á, Kovács M, Magyar J, Németh L, Ricsóy M, Gádoros J, Balázs J. (2009) A napi időbeosztás és az életminőség vizsgálata pszichiátriai zavarban szenvedő

gyermekeknél. Psych Hung XXIV (Suppl): 19-19

Balazs J, **Dallos Gy**, Gadoros J. (2009) Age related differences on the prevalence and patterns of comorbid conditions of children and adolescents with attention-deficit hyperactivity disorder. ESCAP, 2009 Budapest all abstracts, O142 pp. 142. http://www.escap.eu/bestanden/Budapest%202009/budapest_2009_all_abstracts.pdf. Utolsó megtekintés 2015.01.04.

Balazs J, **Dallos Gy**, Gabor R, Kovacs M, Nemet L, Ricsoi M, Gadoros J. (2009) Gender differences across age in the admission rate to a child-, and adolescent psychiatric department of Hungary. ESCAP, 2009 Budapest all abstracts, P324 pp. 324. http://www.escap.eu/bestanden/Budapest%202009/budapest_2009_all_abstracts.pdf. Last access: 04.01.2015.

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