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Familial variables as predictors of psychological maladjustment in Lithuanian children with phenylketonuria

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Background:	Summary Children with phenylketonuria of early onset under continuous treatment are considered at higher risk for psychological maladjustment than children without other chronic diseases. The aim of the present study was to evaluate the psychological adjustment of Lithuanian children with treated phenylketonuria and analyze it in the context of the psychological adjustment of their parents.
Material/Methods:	The parents of 37 early-treated children (age 4–14 years old) with phenylketonuria and of 37 matched controls were asked to fill out the Child Behavior Checklist and questionnaire on stress coping strategies. Parents of children with phenylketonuria answered a questionnaire on reactions to the child's disease and its impact on the family.
Results:	Lithuanian children with treated phenylketonuria have significantly more emotional and behavioral problems than healthy controls. They are more withdrawn, anxious/depressed, have more social and attention problems. The higher rates of internalizing and total problems are related to parental maladjustment (feelings of guilt and anger) together with maladaptive (emotional) everyday stress coping strategies. These last two factors promote overindulging the child, which is also a predictor of psychological maladjustment in children with phenylketonuria.
Conclusions:	The already existing organic vulnerability may account for the greater susceptibility of children with phenylketonuria to psychological risk factors, as for example parental inability to cope adequately with everyday stress related to the demands of disease and its treatment.
key words:	phenylketonuria • psychological adjustment • children • chronic illness
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BACKGROUND

Phenylketonuria (PKU) is an inherited metabolic disease which, if untreated, is associated with severe mental retardation. The absence or inactivity of phenylalanine hydroxylase, the enzyme that converts the amino acid phenylalanine (Phe) to tyrosine, causes PKU. This conversion of Phe is important for the biogenesis of several neurotransmitters, including dopamine and serotonin, and prevents the accumulation of neurotoxic metabolites. Lifelong dietary treatment is recommended for all patients with PKU from birth to avoid mental retardation. The dietary treatment involves the severe restriction of natural proteins and supplementation with phenylalanine-free amino-acid formulas.

In Lithuania newborn screening for PKU was introduced in, 1975. The incidence rate of this autosomal recessive metabolic disorder is 1 in 9300 newborns in the Lithuanian population [1].

Even early detected and continuously treated patients with PKU have a higher risk for psychosocial maladjustment [2]. Children and adolescents with PKU aged 8 to 18 years have been reported to have more internalized problems (e.g. depressive mood, withdrawn behavior, anxiety) and hyperactivity than healthy controls or the general population [3–8]. The rates of externalizing problems in children with PKU are not higher than those in normal controls [2,9].

There are two hypotheses concerning the etiology of the elevated rate of psychosocial maladjustment in phenylketonuria, one based on biological factors, and the other on psychological considerations.

From the biological point of view, increased levels of phenylalanine may lead to a reduced synthesis of dopamine and serotonin in the brain of patients with PKU, resulting in an imbalance of neurotransmitters and thus contributing to the pathogenesis of psychiatric disturbances [7,10,11]. Resulting defects in the frontal lobes can be the cause of behavior problems, e.g. hyperactivity and impulsiveness [5,12]. Several studies have suggested that lower IQ can be a factor in psychological maladjustment in early treated PKU patients [9,13]. A study conducted with 25 Lithuanian children with PKU ranging in age from 7 to 11 years revealed that lower IQ associated with elevated Phe level, not the mean Phe level itself, contributes to the internalizing problems of children with PKU [14]. Lower IQs in children with PKU, a common finding among those with higher Phe levels, increase the likelihood of anxiety/depression and withdrawal.

The psychological perspective stresses the impact of abnormal developmental conditions and stress evoked by the burdensome continuous dietary treatment [8,15]. Beyond the intrachild focus of most organic models, contemporary frameworks for studying child development increasingly emphasize the importance of interacting biological, social and psychological factors. Central to these current perspectives is the recognition of the family as the critical context of development for the

young child [16]. Parental involvement in PKU treatment is essential, because the parents are mostly responsible for the child maintaining a proper diet.

In addition to the usual strain associated with caring for a newborn child, the parents of PKU children have to deal with two additional demands: 1) the grief and disappointment of having given birth to a sick child, 2) demands associated with learning to manage the diet [17]. Implications from work with handicapped groups suggest that the parents' interactions with their child with PKU are affected by parental feelings of guilt [18]. Distress and anxiety, common in PKU families, especially in the first year, may be the cause of neurotic or psychosomatic problems found in affected children [5]. Also, a restrictive-controlling style of parenting is believed to contribute to the development of psychosocial maladjustment [2,9]. Only a few studies, however, have explored the psychological adjustment of children with PKU in the context of family-related factors. Such investigations could shed some light on environmental factors that covary with measures of psychological functioning across the lifespan of patients with early treated PKU [9].

The aim of this study is to evaluate the behavioral and emotional problems in Lithuanian children with phenylketonuria and to analyze the probable reasons for these problems in the context of parental psychological adjustment to the child's illness.

MATERIAL AND METHODS

37 Lithuanian children with PKU (age 4–14, mean 9 years; SD 2.84; 20 female, 17 male) and their parents participated in this study, along with the parents of 37 healthy children without common chronic illness, matched by age, sex and familial characteristics. The children with PKU are patients of the Vilnius University Hospital Medical Genetics Center. The inclusion criteria included especially parental agreement to participate in the study, the absence of mental retardation in the child, and treatment started early and continued without interruption.

The children's psychological adjustment was assessed from parents' ratings on the Lithuanian-language version of the Child Behavior Checklist (CBCL) [19]. The CBCL measures problems on 8 subscales of behavior syndromes, including internalizing problems (withdrawal, somatic complaints without medical reasons, and anxiety/depression), externalizing problems (delinquent, aggressive behavior), social problems, thought problems, and attention problems.

The parents' strategies for coping with stress were assessed with the Lithuanian-language version of the Coping Strategies Questionnaire designed by A. Elklit (1996), which measures adaptive coping (rational and detachment strategies) and maladaptive coping (emotional and avoidant) in stressful everyday life situations [20].

Parental adjustment to the child's disease and relations with the sick child were evaluated by a structured ques-

Table 1. CBCL scores for children with phenylketonuria and healthy controls (means and standard deviations).

CBCL scale	Children with PKU		Healthy controls		t	p
	Mean	SD	Mean	SD		
Withdrawal	4.68	2.68	3.11	1.79	2.960	0.004
Somatic complaints	2.97	2.18	1.84	1.79	2.450	0.017
Anxiety/depression	6.89	3.97	4.3	2.76	3.265	0.002
Social problems	4.11	2.27	2.81	1.94	2.642	0.010
Thought problems	0.89	1.54	0.46	0.77	1.527	0.131
Attention problems	7.35	3.76	4.51	2.35	3.893	0.001
Delinquent behavior	3.19	2.2	2.65	1.81	1.154	0.252
Aggressiveness	11.57	5.32	8.6	4.75	2.535	0.013
Internalizing problems	14.08	7.26	8.89	4.97	3.588	0.001
Externalizing problems	14.76	6.77	11.24	6	2.363	0.021
Total problems	46.03	18.36	32.62	14.57	3.480	0.001

Table 2. Mean and standard deviations of stress coping strategies scores for parents of PKU-affected children and for parents of healthy controls.

Coping strategies	Mean (SD)		t
	Parents of children with PKU	Parents of healthy controls	
Rational	18.38 (4.57)	18.86 (4.92)	0.421
Detachment	6.19 (2.38)	7.6 (2.94)	2.235*
Emotional	8.19 (3.35)	7.6 (2.68)	0.845
Avoidance	13.75 (4.59)	14.27 (3.41)	0.551
Total adaptive	24.47 (5.84)	26.56 (6.17)	1.450
Total maladaptive	21.94 (6.01)	21.87 (4.67)	0.063

* p<0.05;

tionnaire which consists of statements answered 'yes' or 'no', such as: 'I felt confused', 'I blamed myself', 'I was angry with God', 'I often argue with the child', 'I indulge the sick child', etc.

Statistical analysis

Statistical analysis of the data was performed with SPSS (Statistical Package for the Social Sciences), version 9.0. The Student t test and Mann-Whitney U-test were used to compare means between groups. Correlations were assessed using Pearson's r criteria. The Chi-squared test was used to assess correlation between variables. Finally, multiple regression analysis was used to determine predictive variables.

RESULTS

A between-group comparison of CBCL scores with the Student t-test shows that children with PKU have significantly more internalizing ($p<0.01$), externalizing ($p<0.05$) and total problems ($p<0.01$). Children with PKU are more withdrawn and anxious/depressed ($p<0.01$), have more somatic complaints ($p<0.05$), social problems and attention problems ($p<0.01$), and are more aggressive ($p<0.05$) than healthy controls (Table 1). There were no significant differences found in CBCL scores between girls and boys in either children with PKU or healthy controls.

Parents who have children with PKU and who have healthy children do not differ significantly in terms of everyday stress coping, except for detachment strategy (Table 2). Parents of healthy children use adaptive coping more often as compared to parents of children with PKU. Additionally, correlational analysis of parental coping and CBCL scores shows different tendencies in both groups. Emotional (maladaptive) coping of parents with healthy children relates only to delinquent behavior ($r=0.387$, $p<0.05$). Emotional coping of parents who have children with PKU relates to children's anxiety/depression ($r=0.392$, $p<0.05$), somatic complaints ($r=0.44$, $p<0.01$) and internalizing problems ($r=0.441$, $p<0.01$).

A summary of parental responses to the child's disease and relations with the child is shown in Figure 1.

The statistical analysis of association between variables with the Chi-squared test shows that parental feelings of anger and guilt are related significantly to indulgence ($\chi^2=9.715$, $p<0.01$ and $\chi^2=8.811$, $p<0.01$, respectively). The tendency of parents to respond to the child's disease with feelings of guilt is related, in turn, to parental emotion-oriented stress coping ($\chi^2=21.117$, $p<0.05$).

The comparative analysis of CBCL scores regarding the reactions of parents who have children with PKU to the child's disease, feelings of anger and guilt and the tendency to be over-indulgent with the child with PKU reveals several significant differences (Table 3). Parents who report feelings of guilt and anger and those who indulge their sick child rate their child as having more internalizing and total problems than those parent who do not report feelings of anger/guilty and do not over-indulge their child. In particular, children with PKU whose parents over-indulge them or/and feel guilty/angry about the child's disease are more withdrawn, more anxious/depressed, and have more social and attention problems (Table 3).

As some PKU-affected children have PKU-affected siblings, we compared the CBCL scores of the former to PKU-affected children who have healthy siblings and those who are the only child in the family. The results of comparison of mean CBCL scores done with the Kruskal-Wallis test reveal significant differences among the three

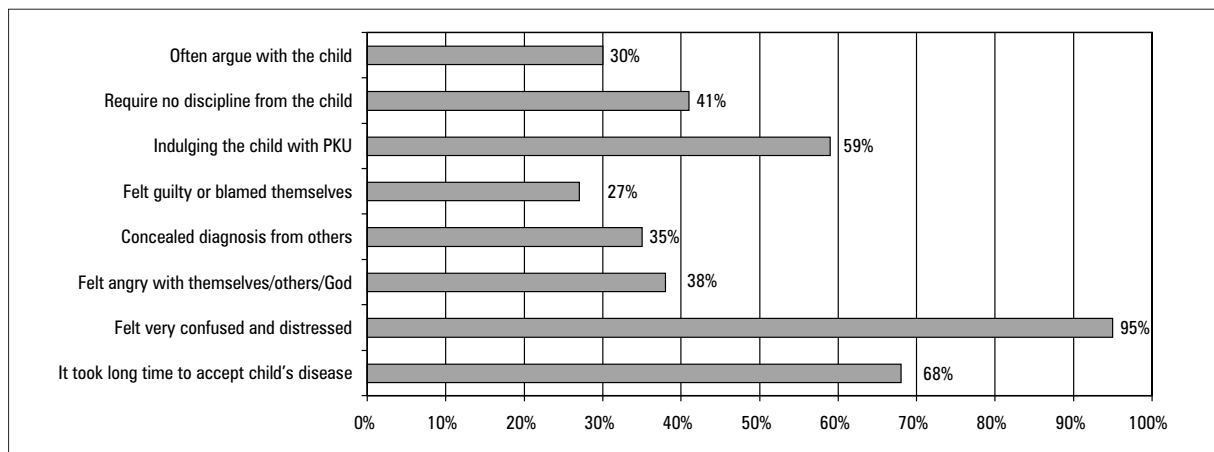


Figure 1. Summary of parental reaction to child's disease and relations with a child.

Table 3. Comparison of CBCL scores of children with PKU according to their parents reactions to child's disease and interactions with a child.

CBCL scale	Mean (SD)		Z value	Mean (SD)		Z value	Mean (SD)		Z value
	Parents felt angry N=14	Parents did not feel angry N=23		Parents felt guilty N=10	Parents did not feel guilty N=27		Parents indulging a child N=23	Parents are not indulging N=14	
Withdrawn	6.21 (2.23)	3.74 (2.53)	2.731**	6.1 (1.66)	3.92 (2.61)	2.477*	5.59 (2.38)	2.86 (1.88)	3.192**
Somatic complaints	3.29 (2.23)	2.78 (2.17)	0.722	4.3 (3.23)	2.46 (1.45)	1.305	3.59 (2.5)	2 (1.18)	1.882
Anxious/depressive	8.71 (5.06)	5.78 (2.68)	1.590	9.4 (4.45)	5.89 (3.46)	2.202*	8.14 (4.25)	4.86 (2.71)	2.236*
Social problems	5.21 (2.19)	3.44 (2.13)	2.260*	5.6 (2.07)	3.58 (2.16)	2.245*	4.82 (2.13)	3.07 (2.2)	2.128*
Thought problems	1.57 (2.24)	0.48 (0.67)	1.604	1.4 (1.35)	0.73 (1.61)	1.957	1.23 (1.86)	0.43 (0.65)	1.406
Attention problems	9.5 (3.48)	6.04 (3.35)	2.644**	9.3 (3.02)	6.69 (3.86)	1.970*	8.41 (3.49)	5.86 (3.84)	1.990*
Delinquent	3.5 (2.25)	3 (2.2)	0.732	3.5 (2.72)	3.12 (2.07)	0.269	2.77 (2.14)	3.93 (2.24)	1.580
Aggressive	12.93 (5.44)	10.74 (5.19)	1.210	13.1 (4.43)	11.31 (5.45)	0.780	12.64 (5.12)	10.5 (5.22)	1.107
Internalizing problems	17.71 (7.89)	11.87 (6)	2.101*	19.2 (7.7)	11.89 (6.13)	2.546*	16.86 (7.24)	9.29 (4.55)	2.989**
Externalizing problems	16.43 (7.01)	13.74 (6.56)	1.083	16.6 (6.48)	14.42 (6.75)	0.534	15.41 (6.6)	14.43 (6.96)	0.276
Total problems	56.07 (19.21)	39.91 (15.17)	2.321*	58.6 (16.22)	41.27 (17.42)	2.564**	51.73 (17.69)	37.21 (16.99)	2.112*

* p<0.05;

** p<0.01

groups (Table 4). Children with PKU who have healthy siblings and who are the only child are more withdrawn, anxious/depressed, and have more attention problems. The mean scores of total problems and internalizing problems in these three groups differ significantly as well. The mean age in these groups does not differ significantly.

We noticed a tendency for parents of children with PKU who have healthy sibling and are the only child to be more prone to indulge their sick child and more often to feel angry and/or guilty in reacting to the child's disease. However, the association between these

variables is not statistically significant as computed by the Chi-squared test.

Multiple regression analysis was used in our study to explore whether the familial variables explored in our study have predictive value for the psychological adjustment of children with PKU. The results of regression analysis show that parental emotional coping and over-indulgence of a child with PKU account for 38% of the variance of internalizing problems in children with PKU (F=9.748, p<0.001, Table 5). None of the variables have significant predictive value for externalizing prob-

Table 4. Mean and standard deviations of CBCL scores for PKU-affected children with PKU-affected sibling, healthy sibling and the only child in the family.

CBCL scale	Mean (SD)			F
	The only child (N=14)	With PKU-affected sibling (N=9)	With healthy sibling (N=14)	
Withdrawal	4.86 (2.07)	2.67 (2.12)	5.79 (2.94)	4.501*
Somatic complaints	3.21 (2.67)	2.67 (1.73)	2.93 (2.02)	0.169
Anxiety/depression	7.57 (2.29)	3.33 (2.29)	8.5 (4.57)	6.480*
Social problems	4.14 (2.07)	2.78 (2.33)	4.93 (2.17)	2.692
Thought problems	0.93 (0.92)	0.00	1.43 (2.21)	2.563
Attention problems	7.07 (3.1)	5.11 (3.37)	9.07 (2.1)	3.453*
Delinquent behavior	3.21 (2.64)	2.44 (1.51)	3.64 (1.51)	0.808
Aggressiveness	12.79 (5.04)	9 (5.61)	12 (5.22)	1.502
Internalizing problems	15.07 (6.1)	8.33 (5.12)	16.79 (7.8)	4.739*
Externalizing problems	16 (7.15)	11.44 (6.33)	15.64 (6.4)	1.472
Total problems	48.43 (14.54)	30.33 (15.64)	53.71 (18.19)	5.899*

* $p < 0.05$;** $p < 0.01$ **Table 5.** Multiple regression analysis predicting children's with PKU internalizing problems.

Predictor variables	β	t	p
Indulgence	0.401	2.703	0.011
Emotional coping	0.348	2.346	0.025
Siblings	0.014	0.098	0.922
Feelings of anger	0.130	0.777	0.443
Feelings of guilt	0.255	1.642	0.111

lems in children with PKU. Only parental reaction to the child's disease with feelings of anger toward self/God/others account for, 19% of variance of total problems (Multiple $R=0.436$; $F=7.729$, $p < 0.01$).

DISCUSSION

Lithuanian children ages 4 to 14 under continuous treatment for phenylketonuria, compared to those who do not have PKU, have more behavioral and emotional problems as rated by their parents. Their higher incidence of internalizing problems is similar to those reported by other researchers [3,5,7]. In addition, the children with PKU evidenced more social and attention problems. These findings are also similar to those of Weglage et al. (2000) and Smith et al. (1988). The finding that our PKU patients are rated higher on aggressive behavior (and overall externalizing problems) is unexamined in previous studies. Moreover, the aggressive behavior was not explained solely by any of the variables explored in our study. We have two possible explanations for higher aggressiveness in children with PKU:

- First of all, there is a tendency for aggressive behavior to co-occur with social and attention problems.
- Secondly, lower intelligence and learning difficulties are known to correlate with children's conduct problems, e. g. aggressive behavior [21]. Our earlier studies on the intellectual functioning of Lithuanian PKU-treated children have revealed their mean IQs to be lower than those of healthy peers [14,22].

The findings of our study in essence confirm the significance of familial factors in predicting the psychological adjustment of children with PKU. Parental maladaptive stress coping and proneness to over-indulge a sick child predict the higher rates of internalizing problems in children with PKU. Thus the presence of restrictive-controlling parenting is considered to pose a risk that children with PKU evidence more behavior problems [2,9]. Parental overprotection is also claimed to play an important role in the psychological functioning of children with chronic illness [18,23]. Both may be conditioned by parental inability to react adequately to their child's disease (e.g. with feelings of anger or guilt). Feelings of guilt and/or anger have no predictive value, though they are related to indulgence and the psychological problems of children with PKU in the present study.

One important consideration based on the limitations of the present study must be discussed. Namely, there is the possibility that parents who react to the child's illness more negatively or are generally maladjusted simply detect more psychological problems in the child. A similar tendency is evidenced in other investigations as well [24–26]. The evaluations of the children's psychological adjustment obtained from other informants (teachers, specialists, older children themselves) could provide more clarity in future studies.

In the present study, very novel and interesting findings were obtained by comparing children with PKU according to their siblings. When there is one more PKU-affected child in the same family, they both have considerably less behavior problems than PKU-affected children growing up with a healthy sibling or being the only child in the family. Probably the reasons for this are not to be found in the dietary treatment itself, but in the fact that these extra treatment requirements influence child-parent and child-sibling relations.

According to Caprara and Rutter (1997), there is a common human tendency to compare oneself in social situations to a significant other [27]. Children as well as

adults are sensitive to all indications as to whether they are being treated better or worse than others. Apart from other possible subtle differences that children may detect in making such comparisons, being fed with different food is most apparent, and may be interpreted as an offence or an injustice.

Parents who cannot give the child the desired food may also feel that they are offending the child. Food and nourishment can be equated with care and love in a psychological sense. That is why parents may be inclined to re-compensate their child by indulging him in other activities or situations. Overindulging the sick child in the case of PKU is also related to the very adherence to dietary requirements, as for example when parents 'pitying' their child allow him/her to eat forbidden food. The resulting increase of the Phe level in the PKU-affected child may in turn contribute to the child's cognitive and emotional dysfunction.

Finally, we accept the interactional developmental perspective, which emphasizes that children's psychopathology can never be viewed as exclusively 'within' the child [27,28]. The already existing organic vulnerability may account for PKU children's greater susceptibility to psychological risk factors. The accumulation of multiple negative stresses and parental inability to cope adequately may further increase the risk for psychopathology in the child while dealing with chronic illness and continuous demands for treatment in everyday life. Thus parental psychological adjustment to the child's chronic conditions and parental coping strategies are important to consider when treating PKU, and should be addressed by means of education, psychological counseling and other forms of assistance.

CONCLUSIONS

1. Lithuanian children treated for phenylketonuria have more internalizing and externalizing problems than their peers without chronic disease.
2. Children with phenylketonuria who have one or more siblings with the same condition have less psychological problems than those who have healthy siblings or are the only child.
3. Parental maladaptive stress coping and over-indulgence of a child predict internalizing problems in children with phenylketonuria.

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