

Personality Characteristics in Patients with Phenylketonuria Treated Early¹

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ABSTRACT. In the course of the German Collaborative PKU Study, the results of the Personality Questionnaire for Children (PFK 9–14) of 58 10-y-old patients treated early for phenylketonuria were analyzed. The main message of our data is that patients with phenylketonuria who were treated early and strictly did not show a higher risk for severe emotional and behavioral maladjustment compared with healthy controls at the age of 10 y. The patients were characterized only by “less masculinity of attitudes.” Because no significant correlations were observed between the quality of dietary control and the results of the questionnaire, the noticed personality characteristic of the patients could be interpreted as a psychosocial consequence of the chronic disease. (*Pediatr Res* 35: 611–613, 1994)

Abbreviations

Phe, phenylalanine
IQ, intelligence quotient
PKU, phenylketonuria
ANOVA, analysis of variance

Up to now only a few studies have dealt with the problem of emotional and behavioral consequences of PKU and its dietary treatment. Children with untreated PKU are typically described as hyperactive, erratic, and aggressive, often with temper tantrums, episodes of screaming, noisiness, and self-punitive behavior (1). Also, children with PKU and normal intelligence who are treated early are reported to have higher risk of psychopathologic disorders or emotional and behavioral difficulties such as mannerism, anxiety, depression, hyperactivity, and low frustration tolerance (2–9). They are also described as less autonomous, less self-confident, and more solitary and unhappy (9, 10).

Earlier studies on the topic of psychosocial maladjustment have varied extensively in design, methods, terminology, and results (10). Findings of most studies are not comparable and generalizable because of severe methodologic problems such as small samples, missing control groups, inhomogeneity of patients concerning age and sex, and insufficient information concerning length and quality of dietary control (10). Most studies are based on outside observations by teachers, parents, or hospital staff (1–9, 11). Only a few studies give an insight into psychic processes of the patients themselves (10). In general, epidemiologic studies and examinations of specific risk groups have demonstrated an increased incidence of psychological maladjustment in children and adolescents with chronic diseases (12–16).

Received April 15, 1993; accepted December 7, 1993.

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Supported by Bundesministerium für Forschung und Technologie (BMFT).

¹This study was done on behalf of the German Collaborative PKU Study. Participating centers were Berlin, Düsseldorf, Hamburg, Heidelberg, Göttingen, München, Münster, and Ulm.

In the literature, different hypotheses exist with regard to a higher rate of psychosocial maladjustment of patients with PKU. First, a neurobiochemical approach suggests that the direct effect of increased Phe levels on brain cells produces an impairment of brain protein synthesis, myelin turnover, and neurotransmitter amine synthesis (8). Second, the psychosocial approach emphasizes that the necessity of maintaining a highly artificial diet, regular blood tests, frequent visits to the hospital, and daily problems managing the diet may contribute to a higher frequency of psychosocial problems (10, 12, 15, 17). Moreover, the parents' perceptions and expectations of difficulties or restrictions associated with chronic diseases may provoke changes in the child's adjustment (3, 6, 12–15). In addition the chronic disease, PKU may mislead parents into becoming overprotective and restrictive with their children, which is found to be a risk factor for psychosocial maladjustment (10).

In a prospective study of patients with PKU who were treated early, we attempted to give an introspective recording of psychic processes where an outside observation does not have access, for instance, to the patients' self-concept, needs, and motives. In addition, we tried to answer whether special aspects of emotional and behavioral development are associated with the quality of dietary control.

MATERIALS AND METHODS

In this study, data of 58 10-y-old patients with classic PKU who were treated early (30 girls and 28 boys) were investigated (18). The diet started on average at the 17th d of life (SD = 7.7; range, 7–45 d).

The patients completed the Personality Questionnaire for Children (PFK 9–14) (16, 19), which gives insight into behavioral patterns, needs, motives, and self-concept of the patients. Out of the 15 primary factors, five superordinate secondary factors were built (Table 1). On the basis of factor analysis, the PFK 9–14 questionnaire was constructed by Seitz and Rausche “for an early identification of children with potentially behavioral and emotional disorders” (16, 19). The PFK 9–14 is the most often used and best evaluated personality questionnaire for 9- to 14-y-old children in German-speaking countries (10, 16, 19, 20). It was developed in 1976 (19), and it was standardized and revised in 1992 (16). The following reliability scores were computed for the scales of the PFK 9–14: the split half-coefficients r_{ii} according to Spearman-Brown ranged from 0.66 to 0.87 (mean $r_{ii} = 0.76$) and the internal consistency scores r_{int} according to Cronbach ranged from 0.67 to 0.87 (mean $r_{int} = 0.74$). The factor-analyzed PFK 9–14 only consists of items that had a communality greater than 0.1 and more than 50% of the communality on one factor. The five secondary factors were the result of a factor analysis based on the intercorrelations of all PFK scales (16). As an indication of validity the constance of factor intercorrelations and structure of factors were replicated for different populations (21–23). The PFK 9–14 was standardized separately for boys and girls and different age groups (9, 10, 11, 12, 13, and 14 y).

Table 1. *Personality Questionnaire for Children (PFK 9-14)*

	PKU group (n = 58)		Comparison group (n = 218)		p*
	Mean	SD	Mean	SD	
Behavioral patterns					
Emotional sensitivity	49.5	8.8	50.0	10.0	NS
Lack of will control	48.1	11.0	50.0	10.0	NS
Extrovert temperament	48.7	9.8	50.0	10.0	NS
Interpersonal behavior	49.1	9.7	50.0	10.0	NS
Needs and motives					
Aggressive need for self-presentation	47.9	11.5	50.0	10.0	NS
Need for autonomy and self-sufficiency	47.1	9.6	50.0	10.0	NS
Scholastic ambition	49.8	10.3	50.0	10.0	NS
Social commitment	50.4	8.3	50.0	10.0	NS
Dependency on adults	49.2	10.3	50.0	10.0	NS
Masculinity of attitudes	43.3	10.5	50.0	10.0	0.001
Self-image					
General anxiety	51.4	8.3	50.0	10.0	NS
Self-confidence	52.6	8.3	50.0	10.0	NS
Impulsiveness/carefreeness	50.5	9.3	50.0	10.0	NS
Self-deception	52.6	8.0	50.0	10.0	NS
Feelings of inferiority	47.6	9.1	50.0	10.0	NS
Secondary factors					
Aggressive assertiveness	48.4	10.0	50.0	10.0	NS
Social complacency	51.9	9.3	50.0	10.0	NS
Emotionality	49.4	8.5	50.0	10.0	NS
Self-sufficient isolation	48.3	8.9	50.0	10.0	NS
Open-optimistic orientation	51.9	8.3	50.0	10.0	NS

* Two-sided *t* test.

The control populations were representative for socioeconomic status and intelligence (16, 19). The patients with PKU were only compared with the 10-y-old male ($n = 110$) and female controls ($n = 108$).

IQ data for 52 patients were available and measured by the German version of the WISC-R at the age of 9 y. Annual medians were computed from quantitative measures of serum Phe concentrations, regularly registered on a monthly basis. The mean of the annual medians was taken as an index of dietary control.

Parametric tests (*t* test, ANOVA, product-moment correlation according to Pearson) were used for statistical evaluation of the data. For the medians of the serum Phe concentrations a cluster analysis according to MacQueen was computed. To evaluate the relationship between the PFK scores and the quality of dietary control two statistical procedures were used. First, correlations according to Pearson were computed to test the general relationship between the continuous variables: PFK scores and serum Phe levels. Second, ANOVA for the three subgroups of cluster analysis should reveal possible differences between the subgroups with "good," "intermediate," and "poor" dietary control. Two-sided tests were computed. The α -error was corrected according to Bonferroni.

RESULTS

Dietary control. According to the German Pediatric Society, serum Phe concentrations for patients with PKU younger than 10 y of age should be below 363 $\mu\text{mol/L}$ (24).

Cluster analysis of the individual longitudinal Phe profiles revealed three clusters of different dietary control (Fig. 1): "good dietary control" cluster ($n = 30$) with mean Phe levels nearly or below 363 $\mu\text{mol/L}$ all the time; "intermediate dietary control" cluster ($n = 22$) with Phe levels surmounting the critical level of 363 $\mu\text{mol/L}$ at the age of 2 y and approaching 606 $\mu\text{mol/L}$ at the age of 9 y; and the "poor dietary control" cluster ($n = 6$) with Phe levels higher than 363 $\mu\text{mol/L}$ after the age of 2 y, higher

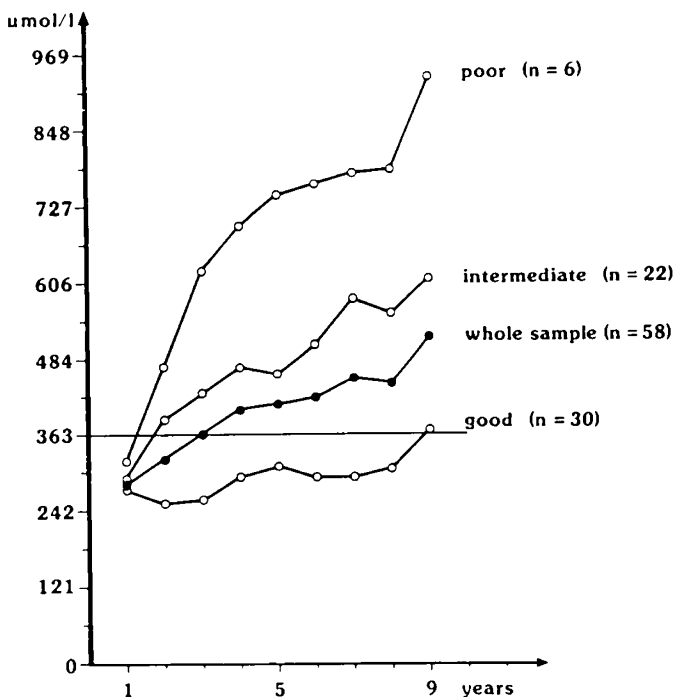


Fig. 1. Serum Phe concentrations: average of annual medians for the whole sample and the subgroups with good, intermediate, and poor dietary control. The horizontal line indicates the desired level.

than 606 $\mu\text{mol/L}$ after 3 y, and ending up with 936 $\mu\text{mol/L}$ at the age of 9 y.

IQ. A total of 52 patients were tested with the WISC-R. With a mean IQ of 96.4 (SD = 12.8; range, 70-122), the patients reached an intellectual performance within the normal range (mean = 100, SD = 15), but it was significantly below the mean IQ of the general population (mean = 100, SD = 15) (*t* test, $p < 0.05$). Patients with poor (mean = 90.0; SD = 7.5; range, 82-102; $n = 5$), intermediate (mean = 92.8; SD = 11.3; range, 70-114; $n = 21$), and good dietary control (mean = 100.7; SD = 13.6; range, 70-122; $n = 26$) had significantly different mean IQ (ANOVA, $F = 3.28$, $df = 2$, $p < 0.05$).

Personality Questionnaire for Children (PFK 9-14). In comparison with healthy controls, the 58 patients with PKU only showed significantly less "masculinity of attitudes" (Table 1). Separate analysis confirmed this significant difference even for the boys' group ($n = 28$) and the girls' group ($n = 30$). No significant differences were observed between the results of the boys' group and the girls' group (*t* test, NS).

Relationships between personality characteristics and quality of dietary control. No significant correlation could be computed between the scales of the PFK questionnaire and the average serum Phe concentration since birth for the whole group ($n = 58$) as well as for the boys' group ($n = 28$) and the girls' group (correlations according to Pearson, NS).

The three groups ("good," "intermediate," and "poor dietary control") did not differ significantly in their personality characteristics (ANOVA, NS).

DISCUSSION

In contrast to other studies, these results suggest that the patients with PKU treated early and relatively strictly do not show a higher risk for severe psychosocial maladjustment compared with healthy controls at the age of 10 y (16, 19). According to their own perception, these children can grow up without increased risks of behavioral and emotional disorders up to the age of 10 y.

One consequence of their experiences with their burdensome

disease might be that they were more sensitive, empathic, and less "masculine in their attitudes." However, they did not believe they were inferior in their general abilities, and they experienced themselves as attractive as their peers. In contrast to other studies, our data do not show that boys were characterized by more severe personality problems than girls (8, 9, 11).

There are several explanations for these surprising results. First, our patients are still children, and they are still living under the protection of their families. In addition to the burdensome diet, developmental crises like puberty may cause more severe emotional and behavioral problems as reported by Weglage *et al.* (10) for adolescent patients with PKU.

Second, participation in the German Collaborative PKU Study provides intensive medical and psychologic counseling for both the patients and the parents. They were seen at least twice a year, and in case of problems they were seen even more often. This treatment could be interpreted as a protective factor. Furthermore, increased experiences in treating patients with PKU might help not just the hospital staff but also patients and parents in their attitude that living with PKU is a more natural thing than it was 10 or 15 y ago. An increased sovereignty in dealing with PKU probably reduces stress and consequently psychosocial maladjustment.

Third, different methods of examination may cause different results. In most studies, ratings by schoolteachers, parents, or hospital staff were used to characterize the psychosocial development of patients (3, 5–9). Selective perception may influence these results. These individuals might know from the literature or hospital staff that the children have a certain risk for psychosocial maladjustment. On the other hand, it is true that self-ratings by the patients—as used in our study—give an insight into psychic processes where outside observations do not have access, but this approach may cause a "super normal construction of personality" (10). In the first case the extent of personality problems possibly is overrated, whereas in the second case they probably are underestimated.

No significant correlations were observed between the results of the Personality Questionnaire for Children and the average serum Phe concentrations since birth. Furthermore, no significant differences were seen in personality characteristics between the three clusters of different dietary control. These results are arguments against the neurobiochemical hypothesis, at least for patients like those participating in our study with mean serum Phe levels below 909 $\mu\text{mol/L}$. Elevated Phe levels may be more critical (10). Most of our patients reached serum Phe concentrations below those reported for patients of other studies (3, 5–9). However, the variance of serum Phe levels was small, and only six patients had a "poor dietary control." Possibly our patients were too young, and a relationship between serum Phe levels and personality characteristics may occur when children get older.

Weglage *et al.* (10) have demonstrated the importance of psychosocial conditions for the quality of dietary control and the psychological development for adolescents with PKU (10). In the German Collaborative PKU Study both patients and parents received intensive psychologic care. As a consequence, more effective coping strategies in dealing with the disease and diet-specific problems probably reduced the frequency of psychologic problems (10). In special cases, social counseling programs and psychotherapy should be offered to parents and patients continually from soon after birth.

The question remains whether "less masculinity of attitudes" is a specific personality characteristic of patients with PKU. We do not know for sure, but we believe not. The characteristic could be interpreted as a consequence of chronic diseases in general (10). The question whether and how the patients develop specific to their PKU can be answered by comparative studies of

patients with other chronic diseases like diabetes. The question whether the rate of emotional and behavioral disturbances will increase when the child gets older should be answered by repeated examinations at appropriate ages. Both questions will be examined in the German Collaborative PKU Study. The main message of our study is that 10-y-old patients with PKU perceive themselves as quite normal with regard to their personality development. It is an important but one-sided result. Further studies should also concern themselves with the reports of persons to whom the children relate most closely because all these people can rate different aspects of psychosocial development, which may all be important for the research question. The studies will provide information not only for patients with PKU but also for patients with other chronic diseases (10, 12–15, 17, 20).

Acknowledgments. The authors thank Prof. Dr. K. Ullrich from the University of Münster and Dr. P. Burgard from the University of Heidelberg for their helpful cooperation.

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