Behavioural and emotional problems in early-treated adolescents with phenylketonuria in comparison with diabetic patients and healthy controls

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Summary: Even early-treated patients with phenylketonuria (PKU) have a higher risk of psychosocial maladjustment. This study was performed to determine whether emotional and behavioural problems are specific in phenylketonurics and whether they depend on the quality of biochemical control. This comparative study covered 42 PKU patients aged 10–18 years (mean 14.7 years) and 42 diabetic patients matched for sex, age and socioeconomic status. Patients’ groups were compared with a control sample of healthy controls (n = 2900) from an epidemiological study. We used the Child Behavior Check List (CBCL) according to Achenbach, intelligence quotient (IQ) test according to Weiss, and monitoring of blood phenylalanine concentrations and HBA1 concentrations. Internalizing problems such as depressive mood, anxiety, physical complaints or social isolation were significantly elevated in both phenylketonuric and diabetic patients, whereas externalizing problems were not. The two patient groups did not differ significantly either in the degree or in the pattern of their psychological profile. In both groups no significant correlations could be computed between the psychological characteristics and the biochemical control, the IQ, and the socioeconomic status. No patient was undergoing psychiatric treatment or psychotherapy. Our results strongly support a psychological perspective for the development of behavioural and emotional problems in both phenylketonuric and diabetic patients. Thus, medical treatment should be accompanied by psychological support for the families.

Behavioural and emotional problems were reported in 1934 in the first publication on phenylketonuria by Fölling, who described patients as anxious, shy, angry, irritated, unsociable, and showing temper tantrums and catatonia (Fölling 1934).
studies published since then can be divided into two main groups. The first group involved untreated patients demonstrating mainly extrovert psychiatric symptoms such as hyperactivity, aggressiveness and unpredictable behaviour, but also introvert symptoms such as anxiety, depressive mood and social withdrawal (Wood et al 1967). The psychiatric symptoms were mainly explained as biochemical consequences of elevated levels of phenylalanine (Phe) and/or its metabolites (Güttler and Lou 1986; Marholin et al 1978; Smith et al 1988; Wood et al 1967). It was demonstrated that introduction of a phenylalanine-restricted diet might lead to a reduction of psychiatric problems, but it was debated whether these symptoms might also be a consequence of mental impairment (Marholin et al 1978). Marholin and colleagues reported data showing that behavioural therapy might be more effective than a low-phenylalanine diet in reducing psychiatric symptoms.

The second group comprises studies in treated patients also demonstrating introvert and extrovert symptoms as well as hyperactivity and lower levels of social competence (Fisch et al 1981; Kazak et al 1988; Realmuto et al 1986; Reber et al 1987; Stevenson et al 1987; Waisbren and Zaff 1995; Waisbren et al 1984). Most of the results were based on parent and teacher ratings, questionnaires and personality inventories. In a study with a large sample of 544 8-year-old patients, Smith and colleagues (1988) described a lifetime phenylalanine-associated higher incidence of mannerism, hyperactivity, anxiety and solitarity. Problems were more frequent in boys. Burgard and colleagues (1994) in the course of the German PKU Collaborative Study reported that their 60 13-year-old patients were twice as likely to show moderate psychiatric disturbances compared with their peers. No PKU-specific diagnosis was determined and no correlation was found between psychiatric disturbances and phenylalanine levels (Burgard et al 1994). In addition, Pietz and colleagues (1997) reported similar results in a study involving 35 adult patients with an age range of 17 to 33 years. At 26%, the overall rate of psychiatric disorders in patients was not significantly different from that recorded in controls (17%). However, the pattern of psychiatric disturbances was different. Externalizing disorders were reduced, whereas internalizing disorders were increased. Diagnoses were predominantly those of depressive type and were more frequent in women. No correlation was found between the severity or pattern of psychiatric disturbances and school education of parents, biochemical control, IQ or the extension of MRI-visible white-matter abnormalities (Burgard et al 1994; Pietz et al 1997).

There are two hypotheses concerning the aetiology of the elevated rate of psychosocial maladjustment in phenylketonuria. The biological perspective is based on the fact that increased levels of phenylalanine may lead to a reduced synthesis of dopamine and serotonin in the brain of PKU patients and that the resulting imbalance of neurotransmitters may contribute to the pathogenesis of psychiatric disturbances (Güttler and Lou 1986; Smith et al 1988). The psychological perspective stresses the value of abnormal developmental conditions and of stress evoked by the burdensome continuous dietary treatment (Awiszus and Unger 1990; Burgard et al 1994; Pietz et al 1997; Weglage et al 1994, 1996). Although recent recommendations advise that dietary treatment of phenylketonuria should be continued up to adulthood or even lifelong (MRC Working Party on Phenylketonuria 1993), many