ORIGINAL PAPER

M. M. T. Hendrikx
L. W. A. van der Schot
F. M. E. Slijper
J. Huisman
A. F. Kalverboer

Phenylketonuria and some aspects of emotional development

M. M. T. Hendrikx (✉)
Department of Child
and Adolescent Psychiatry,
Academic Medical Centre,
Tafelbergweg 25,
NL-1105 BC, Amsterdam,
The Netherlands

L. W. A. van der Schot
Department of Medical Psychology,
Academic Hospital,
Nijmegen, The Netherlands

F. M. E. Slijper
Department of Child
and Adolescent Psychiatry,
Sophia Children Hospital,
Rotterdam, The Netherlands

J. Huisman
Department of Medical Psychology,
Free University Hospital,
Amsterdam, The Netherlands

A. F. Kalverboer
Laboratory for Experimental Clinical
Psychology, State University Groningen,
The Netherlands

Abstract Early dietary treatment of phenylketonuria (PKU) prevents intellectual retardation and gross neurological impairment although not all neuropsychological problems. This study investigates to what extent the illness and its treatment imposes a burden on emotional development of early-treated PKU patients and on rearing practices of their parents. It is concluded that in early-treated PKU it is particularly difficult to find constructive ways to adapt to the situation for children as well as for parents. As coping with PKU and its treatment is so complicated, paediatric control should be combined with psychocounselling.

Introduction

Early treatment of phenylketonuria (PKU) is highly effective in preserving general intellectual abilities [6, 11, 19] but many authors have reported neuropsychological/cognitive dysfunction [5, 8, 9, 12, 14–16, 20]. Little is known about effects of treatment on personality development. Aspects of family functioning and emotional development secondary to treatment may add to the problems [2]. Changes that start as integrated responses to diet adherence may end up as rigid routines [13]. Tensions may run high. Small children cry when blood is taken and levels of phenylalanine (phe) are often awaited with great anxiety,

fear of mental retardation always being present. One relevant observation in our group is that many patients learn to control their diet at a remarkably young age. From 4 or even 3 years onward most of them are able to refuse food offered to them by kind but unaware people. This precocious selfcontrol is obviously adaptive from a dietary point of view but we doubt whether the same is true in a psychological sense.

The aim of this study was to explore some aspects of behavioural and emotional development in early-treated children with PKU and of rearing practices of their parents. To discriminate between neuropsychological/cognitive and emotional dysfunction we first investigated impulsivity as a cognitive style, expecting children with PKU

to be more impulsive then non-PKU children. Secondly, we investigated rearing styles of parents, expecting parents of PKU children to exert stricter rearing practices than parents of non-PKU children. Thirdly, we questioned parents on their perceptions of their children, expecting parents of children with PKU to perceive their children as more hyperactive, less socially competent and as having more behaviour problems than other parents. Fourthly, we asked the children about their own views on their illness and lastly we asked the children about depressive feelings and feelings of selfesteem, expecting children with PKU to be more depressed and have lower selfesteem then healthy children. Because of the possibility that effects of chronic illness have a general nature and are not PKU-specific we also investigated children with diabetes mellitus (DM).

Patients and methods

Patients

We invited all early-treated PKU patients and their parents in four academic hospitals who were between 9 and 13 years of age. We also invited all DM patients in our hospitals that were diagnosed before the age of 4 years and were of the same age as our PKU group. Of the invited families, 64% and 58% respectively participated. We interviewed all non-participants. Non-participation depended on practical circumstances such as summer vacation and distance in all cases. The PKU group consisted of 12 girls and 10 boys ($n = 22$). The DM group consisted of 8 girls and 6 boys ($n = 14$). In the PKU group mean I.Q. is 92.09 (WISC-R dutch validation). In the DM group I.Q.'s were lacking. However, all children attend normal schools. Normgroups are mentioned below under measures.

Measures

Impulsivity as a cognitive style of problem solving characterized by poor inhibition (an indication of neuropsychological dysfunction) was measured with the widely used matching familiar figures test [7]. Testscores of 77 healthy dutch children of the same age range were used as norms.

Restrictiveness as a generalized rearing style was measured by the child rearing practices report which was developed by Block and Block [3] and adapted to the dutch situation by Dekovic [4]

whose control children were used as normgroup. From this questionnaire we also used the nurturance scale (nurt, expression of warmth, acceptance, understanding). Hyperactivity, social competence and behaviour problems as perceived by parents is measured by the child behaviour check list-parents form (CBCL) as developed by Achenbach [1] and adapted to the dutch situation by Verhulst et al. [18] who also assessed norms for the dutch population.

Evaluation of illness (EvIl) by children with either PKU or DM was investigated with a self-report questionnaire we developed for this study. The EvIl consists of 23 items on a 4-point scale (never-sometimes-often-always). The content of the items describes thoughts and feelings about either PKU or DM (parallel forms) such as "If you have PKU you are never-sometimes-often-always unhappy" or "If one has PKU one has never-sometimes-often-always difficulties in life" or "When I was little and blood was taken I never-sometimes-often-always had to cry". Thus items ask the child to estimate the severity of consequences of the illness for daily, social and future life.

Depression was assessed by the depression questionnaire for children (DQC) which has dutch norms [21].

Selfesteem (IN) was measured with the dutch personality questionnaire for children, inadequacy-scale (IN, vague physical complaints, depressed mood, vague fears and feelings of insufficiency). From this self-report questionnaire we also used the social inadequacy-scale (SI, avoidance of and feeling unhappy in social contacts). These scales have dutch norms [10].

Statistics

We used t-tests for differences in means, one-tailed for all data. To measure the strength of relationships between variables we computed product moment correlation coefficients.

Results

T-test results on all variables but EvIl (because of unavailability of norms, see below) are presented in Table 1. Within the PKU group results are significant on impulsivity as a cognitive style, restrictiveness and nurturance as rearing styles, hyperactivity and social competence according to parents, and selfesteem. The DM group differed from population norms only on social competence according to parents. Direct comparison of PKU and DM groups (no table, data available on request) revealed significant differences on nurturance (P 0.001) and on evaluation of illness (P 0.01), although some other differences

Table 1 T-tests for significance of mean differences. Impulsivity (IMP), restrictiveness (Restr), nurturance (Nurt), hyperactivity according to parents (Hyp-p), social competence according to parents (SC-p), behavior problems according to parents (BP-p), depression (DQC), selfesteem (IN) and social inadequacy (SI) between PKU and normgroup and between DM and normgroup

$*P<0.01; **P<.001$

	Norm	PKU mean	SD	t-value	DM mean	SD	t-value
IMP	–0.19	0.65	1.22	2.36*	–0.09	1.68	0.18
Restr	2.97	3.49	0.80	3.02*	3.10	0.84	0.53
Nurt	5.18	5.45	0.36	3.49**	4.88	0.50	–2.17
Hyp-p	2.96	6.36	5.25	3.03*	4.36	3.56	1.52
SC-p	20.36	16.73	3.89	–4.40**	16.36	3.79	–4.03**
BP-p	19.97	24.09	14.68	1.32	26.50	19.57	1.33
DQC	21.00	21.59	13.71	0.06	18.00	9.32	–0.93
IN	14.48	19.64	8.53	2.77*	17.07	7.62	1.22
SI	11.40	11.73	5.14	0.30	11.29	5.22	–0.08

Fig. 1 Significant correlations
within the PKU group
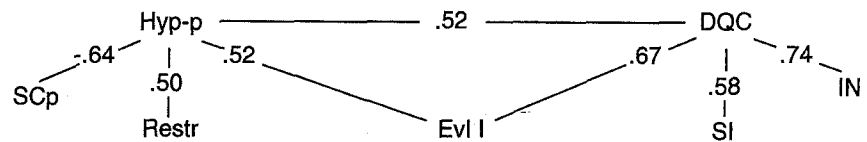
approached significance (IMP P 0.08, Restr P 0.10, Hyp-p
P 0.09). Figure 1 presents a hypothetical clustering of all
significant correlations found between variables within
the PKU group. There were no significant correlations be-
tween I.Q. and any of the variables (data available on re-
quest).

Discussion

Our questions concerned primarily emotional problems
secondary to the nature and treatment of PKU. Interac-
tions between emotional and neuropsychological factors
may be ongoing but they may also be independent. The
concept of impulsivity for instance has more than one
meaning. One is a cognitive style, a concept that is easily
associated with supposed neuro(psycho)logical impair-
ment. A second meaning of impulsivity is uncontrolled
behaviour, i.e. inability to delay gratification [17], rest-
lessness, hyperkinesia. In hyperactivity according to DSM
III-R criteria (diagnostic and statistical manual of mental
disorders) both types of inhibition problems – as they are
usually seen – are present. The "uncontrolled behaviour"
type of impulsivity leads to troublesome behaviour that is
hard to rule for parents though not necessarily antisocial
or even disobedient. This is in fact what was found in the
Smith et al. [14] study using the Rutter behaviour ques-
tionnaire (schoolteachers report). Here "hyperactivity" is
described as "fidgety, restless and cannot settle". In our
study we found high scores on "impulsivity" as a cogni-
tive style as well as on "hyperactivity" (parents report on
behaviour) in PKU patients. However we did not find a
relation between these two (r 0.13) nor between "impul-
sivity" and any of the other behavioural/emotional vari-
ables. This strengthens our belief that in early-treated
PKU, possible brain damage resulting in neuropsycholog-
ical/cognitive dysfunctioning – as in "impulsivity" – may
be present independent of emotional/behavioural difficul-
ties stemming from an illness and its treatment that are in-
herently stressfull. To study this hypothesis in more detail
Phe levels should be included and multivariate analysis
carried out (requiring a greater number of subjects). We
found low selfesteem in PKU children (Table 1). Accord-
ing to their parents they were more "hyperactive" and less
socially competent than healthy children. These parents
exerted more restrictive as well as more nurturant rearing
practices than parents of healthy children. Compared to
DM children some of the differences remained (see re-
sults). Moreover evaluation of illness was significantly
more negative in PKU children than in DM children. Our

expectation that PKU children (and their parents) suffer
and that this suffering is in some ways specific to early-
treated PKU was confirmed. There are several possible
explanations. One is indicated by the correlation found (in
PKU not in DM) between Hyp-p and Restr. We might per-
haps theorize that when parents of early-treated PKU pa-
tients perceive their childs behaviour as "uncontrolled"
(see above) – whether this is a correct perception or not –
they may respond by being more restrictive, presumably
to restore a desired level of control. This rearing style may
be a generalization of necessary dietary control. The Shul-
man et al. [13] study found parental perception – of child
depression in their case – to be of influence on their func-
tioning as a parent. The result on restrictiveness may be in
line with this. An alternative more comprehensive expla-
nation is illustrated by the clustering of significant rela-
tions in Fig. 1: the left side of Fig. 1 contains parental per-
ceptions of child behaviour and restrictive rearing style.
The right side contains feelings of the children. In PKU
paediatricians strongly instruct parents to supervise their
childs diet. There is no direct physical feedback of non-
compliance, only fear of irreversible mental retardation.
This way parents are made fully responsible for their
childs physical and mental development. Awiszus and
Unger [2] found PKU parents to be in conflict between
striving for ideal Phe levels and striving for a healthy per-
sonality development of their child. According to our data
PKU parents were both restrictive and nurturant. Nor-
mally these rearing styles are negatively related (as they
were in DM parents r –0.66). In PKU parents they were
not (r –0.00), possibly reflecting inner conflict. In DM
paediatricians stimulate patients from a relatively young
age onward to selfcontrol of their treatment (dieting and
injections) thus partly taking it out of parents' hands.
Noncompliance leads to direct physical feedback and con-
sequences are usually reversible. Perhaps paediatricians
(different instructions) and parents (different rearing
styles) and children (different evaluation of illness) all
feel differently about PKU and DM respectively. Each
party in this triangle may have (unconsciously perhaps)
slightly different priorities depending on position and re-
sponsibilities.

The correlations in Fig. 1 between IN, SI and DQC (de-
pression) are probably due to overlap as IN and SI con-
cern depressive feelings about specific parts of mental life
(selfesteem and social inadequacy). The relation between
DQC and Hyp-p (contradictory as depression usually re-
lates to lack of activity) is confounded by EvII (adjusted r
0.27), leaving EvII to be the stronger connection between
the parent and child cluster. More research needs to be

done on the relationship between parental rearing styles and perceptions of the child and their childrens' selfperceptions.

Both PKU and DM parents considered their child-patient as less socially competent than healthy children. Social competence on the CBCL concerns degree of social participation, in clubs, with friends or with other people. It is probably true that chronic patients are generally more withdrawn than healthy people. Neither group classified their children as having behaviour problems. As behaviour problems on the CBCL are well known behaviour and/or emotional problems with a fairly high prevalence (at least 5%) in the general population; this means that parents in our groups did not see their child as having any psychopathological problems. PKU parents found their children hyperactive and difficult to restrict and socially less competent and more in need of nurturance than DM parents but they did not find them "ill-willed" or "emotionally disturbed". Smith et al. [14] advocated stricter Phe control. The British PKU patients in cohort 2 of the extensive Smith study were born between 1972 and 1977

and received treatment before 4 months of age. Our patients, born between 1981 and 1985, were all treated before 20 days of age. Control of Phe levels has been very frequent. It may be difficult to further improve on Phe level without raising undue anxieties. One other point needs mentioning. We cannot correct for intelligence as we have no controls (only standards) and no I.Q.'s for the DM group. Within the PKU group, however, correlations between I.Q. and any of the other variables were insignificant and low. This does not preclude relations but it is improbable that all variance in our data could be explained by intelligence.

We conclude that in early-treated PKU it is particularly difficult to find constructive ways to adapt to the situation for children as well as for parents. It seems necessary to combine paediatric treatment with psychocounselling, aimed at better insight in and working through of the elaborate consequences of PKU.

References

1. Achenbach TM, Edelbrock C (1983) Manual for the child behavior check list and revised behavior profile. University of Vermont, Burlington
2. Awiszus D, Unger I (1990) Coping with PKU: results of narrative interviews with parents. Eur J Pediatr 149 [Suppl 1]: 45–51
3. Block JH, Block J (1980) The role of ego-control and ego-resilience in the organization of behavior. In: WA Collins (Ed) The Minnesota Symposia on Child Psychology 13: 39–101
4. Dekovic M (1989) Measuring dimensions and patterns of childrearing: dutch version of the block child rearing practices report (CRPR). Catholic University Nijmegen
5. Fishler K, Azen CG, Henderson R, Friedman EG, Koch R (1987) Psychoedu- cational findings among children treated for phenylketonuria. Am J Ment Defic 92: 65–73
6. Huisman J, Schot LWA van der, Hendrikx MMT, Kalverboer AF, Slijper FME (1992) The interlectual development of patients with phenylketonuria; 15 years screening in the Netherlands (in Dutch). Ned Tijdschr Geneeskd 136, 46: 2277–2281
7. Kagan J, Rosman BL, Day D, Albert J, Philips W (1964) Information processing in the child: Significance of analytic and reflective attitudes. Psychol Monogr; 78
8. Koch R, Azen C, Friedman EG, Williamson ML (1984) Paired comparisons between early-treated PKU children and their matched sibling controls on intelligence and school achievement test results at eight years of age. J Inherited Metab Dis 7: 86–90
9. Koff E, Boyle P, Sigfried M, Pueschel SM (1977) Perceptual-motor functioning in children with phenylketonuria. Am J Dis Child 131: 1084–1087
10. Luteijn F, Dijk H van, Ploeg FAE van der (1989) of the Dutch personality questionnaire for children (in Dutch). Swets and Zeitlinger, Lisse, the Netherlands
11. Primrose DA (1983) Phenylketonuria with normal intelligence. J Ment Defic Res 27: 239–246
12. Realmuto GM, Garfinkel BD, Tuchman M, Tsai MY, Chang PN, Fisch RO, Shapiro S (1986) Psychiatric diagnosis and behavioral characteristics of phenylketonuric children. J Nerv Ment Dis 174(9): 536–540
13. Shulman S, Fisch RO, Zempel CE, Gadish O, Chang PN (1991) Children with phenylketonuria: the interface of family and child functioning. Dev Behav Pediatr 12(5): 315–321
14. Smith I, Beasley MG, Wolff OH, Ades AE (1988) Behavior disturbance in 8 year old children with early treated phenylketonuria. J Pediatr 112(3): 403–408
15. Sonneville LMJ de, Schmidt E, Michel U, Batzler U (1990) Preliminary neuropsychological test results. Eur J Pediatr 149: S39-44
16. Stevenson JE, Hawcroft J, Lobascher M, Smith I, Wolff O, Graham PJ (1979) Behavioral deviance in children with early treated phenylketonu- ria. Arch Dis Child 54: 14–18
17. Taylor EA (1986) The overactive child. Clinics in developmental medicine 97. Blackwell, Oxford
18. Verhulst FC, Akkerhuis GW, Althaus M (1985) Mental health in Dutch children: (I) a cross-cultural comparison. Acta Psychiatr Scand 72 [Suppl 323]
19. Waisbren SE, Mahon BE, Schnell RR, Levy HL (1987) Predictors of intelligence quotient and intelligence quotient change in persons treated for phenylketonuria early in life. Pediatrics 79(3): 351–355
20. Welsh MC, Pennington BF, Ozonoff S, Rouse B, McCabe ERB (1990) Neuropsychology of early-treated phenylketonuria: specific executive function deficits. Child Dev 61: 1697–1713
21. Wit CAM de (1987) Depression questionnaire for children (in Dutch) (DVK). Acco, Amersfoort