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Behavioural and emotional disturbances in people with Prader–Willi Syndrome

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Abstract

Background The study of the behaviour profile in subjects with Prader–Willi Syndrome (PWS).
Methods A total of fifty-eight 3- to 29-year-old subjects with PWS were studied using a standardized parent report of behavioural and emotional disturbances.
Results There was an increase of behavioural and emotional disturbances for the adolescent and young adult age range, whereas gender and intelligence were not significant. Increasing body mass index (BMI) was also associated with more behavioural and emotional disturbances. There was no significant relation between genetic status and behavioural abnormalities.
Conclusions This systematic study supports single case observations of a heightened psychiatric vulnerability of adolescent and young adult PWS subjects.

Keywords age, behaviour, body mass index, Prader–Willi Syndrome

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Introduction

Prader–Willi Syndrome (PWS) is the most common genetic syndrome associated with obesity and has an estimated prevalence of 1/10 000–1/15 000. The presenting symptoms in the neonatal period include hypotonia and feeding difficulties with failure to thrive. This is followed by early onset hyperphagia leading to obesity, hypogonadism associated with genital hypoplasia and pubertal insufficiency is present in most subjects. PWS has a characteristic appearance including short stature. The subjects show a developmental delay with ultimate intellectual impairment, usually with mild intellectual disability (ID). PWS is caused by the deficiency of paternally contributed genes in the proximal long arm of chromosome 15, maternal uniparental disomy, or, rarely, by an imprinting defect (Gunay-Aygun *et al.* 1997). Consensus diagnostic criteria are available (Holm *et al.* 1993).

Besides the mild ID or borderline intelligence, there is some evidence for a characteristic behaviour profile in PWS subjects that becomes evident in childhood. Frequent behaviours include temper tantrums, stubbornness, manipulative and controlling behaviour, obsessive–compulsive features, and difficulties with change in routines (Dykens *et al.* 1996;

State *et al.* 1999). Recently, obsessions and compulsions were studied specifically in two samples of PWS children and adults and a high prevalence of these symptoms was found (Dykens *et al.* 1996; State *et al.* 1999; Dimitropoulos *et al.* 2001). In approximately 5–10% of adult PWS subjects, there is evidence of psychotic disorder. The behavioural problems interfere with quality of life and are a frequent cause of hospitalization and medication use in adults with PWS. The most frequent psychiatric diagnoses are schizophrenia, manic-depressive illness, and obsessive–compulsive disorders (Gunay-Aygun *et al.* 1997). A recent study on problem behaviours and personality compared PWS children and adolescents to clients consulting mental health centres. There were some differences according to parental reports and personality profiles that were specific for internalizing and externalizing problems of PWS subjects (van Lieshout *et al.* 1998).

The present report is based on a relatively large cohort of German and Swiss PWS subjects covering a relatively wide age range, allowing the study of the following issues: (1) developmental effects in terms of age, gender, and intelligence on the behaviour of these subjects; (2) the relation between genetic status and behaviour; and (3) the association of body mass index (BMI) and behaviour.

Method

Sample

The study is based on a total of 58 PWS subjects that were diagnosed in two German and Swiss centres, respectively, by paediatric and genetic experts according to the above-mentioned consensus diagnostic criteria and molecular biological findings. In addition, parents of two self-help groups in Germany and in Switzerland provided data for the present study. There were 28 (48.3%) male and 30 (51.7%) female subjects in the sample. The age ranged from 2 to 29 years with a mean of 12.05 (SD = 7.5) years. Intelligence and developmental test findings were only available for 35 subjects. These data were lacking predominantly in the self-help group subjects. Because of the heterogeneity of tests, only broad bands of intelligence were considered for analyses. Accordingly, the following distribution of intelligence was obtained: 4 subjects (6.9%) showed normal intelligence, 8 (13.8%) functioned in the borderline range, 16 (27.6%) were mildly intellectually disabled, 7 (12.1%) showed severe ID, and data were missing in 23 (39.7%) subjects.

In order to study age and developmental effects, the total cohort was divided into three age groups: subjects aged less than 7 years (preschool children, $n = 19$), subjects aged 7–13 years (primary school-aged children, $n = 16$), and subjects aged more than 13 years (adolescents and young adults, $n = 23$). Full genetic information was available only in 47 out of the 58 subjects. Paternal deletions were found in 28 subjects and maternal uniparental disomy (UPD) was proven for 10 subjects. Imprinting accounted for one patient, and a positive methylation test was only available for eight subjects. The rest of the 11 subjects from the self-help group only had clinical diagnoses. For each subject, the BMI was available. Scores ranged from 13.0 to 54.6 (mean = 25.5, SD = 10.7).

Procedure

The parents of the PWS subjects were asked to respond to the Developmental Behaviour Checklist (DBC) by Einfeld & Tonge (1992, 1995). This is a standardized instrument completed by lay informants to assess behavioural and emotional disturbance in children and adolescents with ID. It covers 96 behavioural items including two open questions that are rated on a three-point scale ranging from 0 to 1 (somewhat or sometimes true) and 2 (very true or often true). The DBC has good psychometric properties (Einfeld & Tonge 1992, 1995) and has also recently been used for the assessment of population prevalence of psychopathology of intellectually disabled children and adolescents (Einfeld & Tonge 1996a,b).

Besides a total score, six subscales based on factorial analyses can be computed. These subscales have been slightly revised based on recent new analyses by the authors (Einfeld & Tonge 1996c). The six subscales are labelled disruptive, self-absorbed, communication disturbance, anxiety, autistic relating, and antisocial. Because of a lack of a standardized scale for the DBC scores, we computed raw scores for the six subscales and transformed them into weighted raw scores (total subscore divided by the number of items of the respective subscale). This procedure allows a comparison of the various subscales among

one another. Statistical analyses included the Fisher Exact Test, both univariate and multivariate analyses of variance, Pearson correlation coefficients, and multiple regression analysis.

Results

Those items that differed significantly among the three age groups are collected in Table 1. Among the total of 96 items, 19 showed significant differences which is more than a chance finding. A large number of items showing a tendency of age effects ($P < 0.10$) are not included in the table. In each subscale, there is some indication that mainly the oldest age group showed the highest rate of abnormalities. Only in a few items (switches light on and off; fussy eater; gorges food; confuses the words of pronouns) it is the very young group of PWS children that showed the highest rate of abnormal behaviour.

The age effect is more clearly evident both for the six subscales and for the total score as shown in Table 2. There was a highly significant effect across age for the majority of the DBC scales. *Post hoc* comparisons by the Scheffé procedure indicated that the increase resulted from the oldest group only. Multivariate analyses showed that age was

Table 1 Distribution of behavioural items with significant age differences

		≤6 years (*n* = 19)		7–13 years (*n* = 16)		>13 years (*n* = 23)		Total (*n* = 58)		Fisher	
Item No.	**Item description**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	**Test**	***P***
Subscale 1: disruptive											
4	Abusive, swears at others	4	23.5	4	22.2	14	60.9	22	37.9	8.12	0.02
37	Irritable	3	17.6	5	27.8	14	60.1	22	37.9	8.56	0.01
82	Tells lies	2	11.8	7	38.9	17	73.9	26	44.8	15.99	<0.001
Subscale 2: self-absorbed											
71	Switches light on and off; or similar repetitive activity	9	52.9	2	11.1	2	8.7	13	22.4	11.26	0.003
93	Wanders aimlessly	–	–	–	–	4	17.4	4	6.9	4.76	0.03
Subscale 3: communication disturbance											
13	Delusions	–	–	–	–	8	34.8	8	13.8	12.33	0.001
83	Thoughts are unconnected	3	17.6	3	16.7	12	52.2	18	37.9	7.40	0.03
Subscale 4: anxiety											
20	Excessively distressed if separated	2	11.8	4	22.2	11	47.8	17	29.3	6.40	0.04
24	Fussy eater or has food fads	5	29.4	3	16.7	–	–	8	13.8	7.66	0.02
37	Irritable	3	17.6	5	27.8	14	60.1	22	32.9	8.56	0.01
84	Tense, anxious, worried	–	–	6	33.3	9	39.1	15	25.9	9.99	0.007
Subscale 5: autistic relating											
16	Doesn't respond to others' feelings	–	–	3	16.7	10	43.5	13	22.4	11.28	0.003
Subscale 6: antisocial											
72	Steals	3	17.6	2	11.1	12	52.2	17	29.3	9.17	0.008
82	Tells lies	2	11.8	7	38.9	17	73.9	26	44.8	15.99	<0.001
Further items											
25	Gorges food, will do anything to get food	10	58.8	8	44.4	21	36.2	39	62.1	11.33	0.003
40	Lacks self-confidence, poor self-esteem	1	5.8	6	33.3	12	52.2	19	32.7	9.96	0.007
55	Prefers the company of adults or younger children	9	52.9	11	61.1	20	86.9	40	69.0	6.20	0.04
64	Scratches or picks his/her skin	7	41.2	13	72.2	19	82.6	39	67.2	7.48	0.02
78	Confuses the use of pronouns	7	41.2	2	11.1	1	4.3	10	17.2	8.69	0.009

Table 2 Developmental Behaviour Checklist Scores for three age groups of Prader–Willi Syndrome subjects

	<7 years (*n* = 19)		7–13 years (*n* = 16)		>13 years (*n* = 23)			
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***F* (d.f. = 2)**	***P***
Disruptive	0.29	0.25	0.37	0.20	0.63	0.48	5.28	0.008
Self-absorbed	0.31	0.26	0.21	0.13	0.32	0.30	1.12	NS
Communication disturbance	0.40	0.25	0.43	0.20	0.65	0.43	3.62	0.03
Anxiety	0.34	0.21	0.44	0.23	0.53	0.31	2.83	0.07
Autistic relating	0.18	0.12	0.26	0.18	0.46	0.32	8.31	0.001
Antisocial	0.18	0.30	0.19	0.20	0.59	0.45	9.61	<0.001
Total score	31.63	16.14	32.25	12.40	50.17	29.90	4.97	0.01

NS, not significant.

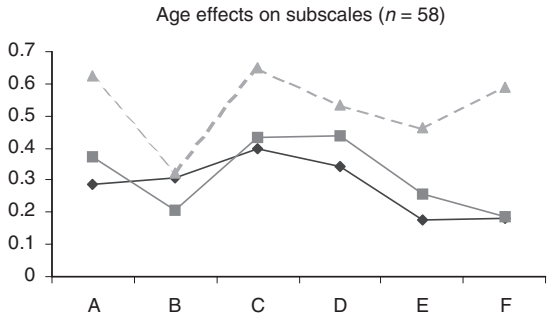

Figure 1 Developmental Behaviour Checklist subscores for three age groups of Prader–Willi Syndrome subjects. A, disruptive; B, self-absorbed; C, communication disturbance; D, anxious; E, autistic relating; F, antisocial; (◆), ≤6 years; (■), 7–13 years; (▲), >13 years.

significant for the entire set of six subscales (Wilks' Lambda = 0.541, $F = 2.82$, d.f. = 12; 94, $P = 0.002$). This general effect results from increased scores for the oldest age group on the following subscales: disruptive, communication disturbance, autistic relating, antisocial, and tendentially, anxiety. Figure 1 shows the DBC subscale profiles of the three age groups. The same significant age effect was also shown for the total score as shown in Table 2. In addition, the same picture emerged when Pearson correlation coefficients were computed. Age correlated significantly with the following subscales: disruptive ($r = 0.34$, $P = 0.01$), communication disturbance ($r = 0.27$, $P = 0.04$), anxiety ($r = 0.24$, $P = 0.07$), autistic relating ($r = 0.52$, $P < 0.001$), antisocial ($r = 0.50$, $P < 0.001$), and total score ($r = 0.41$, $P = 0.001$).

Gender effects were also analysed in both data sets. Gender did not turn out to have any effect on either the total or any of the six DBC subscales. In the same way no significant association between intelligence level and behavioural scores was found in 35 subjects. Furthermore, the relation between genetic status and behaviour was studied. Two subgroups were considered, namely, those with either paternal deletions ($n = 28$) or maternal uniparental disomy ($n = 10$). Both MANOVA for the six subscales and ANOVA for the total score indicated no significant effect for genetic status on behavioural scores.

However, when correlation coefficients between BMI and total and subscale scores were computed, there was a significant association between BMI and the DBC total score, indicating that behavioural abnormalities increase with higher BMI ($r = 0.37$, $P = 0.01$). This association mainly results from an increase of abnormalities in the following subscales: disruptive ($r = 0.37$, $P = 0.01$); autistic relating ($r = 0.64$, $P < 0.001$); and antisocial ($r = 0.42$, $P = 0.004$). When age, gender, genetic status, and BMI were used as predictors of the DBC total score in multiple regression analysis, the multiple regression coefficient was $R = 0.41$ with none of the four variables being statistically significant anymore except a trend for BMI (Beta = 0.39, $P < 0.10$).

Discussion

This study is based on a relatively large cohort of PWS subjects covering the age periods of childhood,

adolescence, and early adulthood. The sample was mainly recruited in two centres of tertiary care. In addition, parents of self-help groups for PWS subjects both in Germany and in Switzerland contributed to the present study. Despite these specific entry criteria, there is no evidence that there is a recruitment bias in the present study, which is based on parents' reports using a standardized questionnaire for behavioural and emotional disturbances in people with ID.

Our findings clearly indicate that adolescence and young adulthood are the critical periods for an increase in behavioural and emotional disturbances in PWS subjects. This is most clearly reflected on the subscale level of the DBC and also documented on the item level. The findings on the item level might be accepted with some caution because of the high number of comparisons and statistical tests being carried out. Whilst a Bonferroni correction of alpha levels was considered to be too harsh in a hypothesis-generating rather than hypothesis-testing study, the emerging alpha levels and the number of statistical differences on the item level point to significant age effects.

The emerging behavioural pattern, with special emphasis on disruptive and antisocial behaviour, is very much in accordance with previous studies (Dykens & Cassidy 1996). However, there is some indication that other problems that have not been studied intensively may also deserve more attention. These problems include communication disturbances, feelings of anxiety, and even features of autistic relating that may become manifest in PWS only by adolescence. However, the abnormalities in relating do not seem to imply a full-blown syndrome of autism.

Our findings also converge with the review statement by Dykens & Cassidy (1996) that gender and IQ level do not appear significantly associated with maladaptive behaviours. Whereas the present study found no behavioural differences in relation to genetic status, a recent study by Dykens *et al.* (1999) observed a dampening of symptom severity because of maternal uniparental disomy. The differences in findings may partly result from the fact that Dykens *et al.* (1999) used age- and gender-matched subjects whereas age and gender were not controlled for in our own analyses because of the small number of only 10 subjects with maternal disomy.

However, there is a clear indication that high BMI scores and high levels of behavioural and emotional disturbances are strongly associated. This association tends to remain even after age, gender, and genetic status are controlled. This finding stands in clear contrast to a recently published study with no association of weight and behaviour problems (Åkefeldt & Gillberg 1999). The latter study, however, used different questionnaires, which are not specifically developed for examining subjects with ID.

In general, our findings, based on a large cohort of PWS subjects, corroborate observations based on single case observations of an increased psychiatric vulnerability in adulthood or with increasing age. This developmental pattern is not specific for either of the two sexes and does not depend on intelligence level, as our analyses clearly showed. The increasing handicap among older PWS subjects might, to some extent, result from the changing pattern of care for these subjects. Nowadays, PWS will probably be diagnosed at an earlier age than in the past so that early intervention will be installed and parents will get support helping them to better cope with their child's disorder. As a consequence, the younger children might suffer from less severe physical and psychological handicaps. The limitations of the study include the lack of formal intelligence testing and genetic information in a sizeable proportion of the sample.

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