Sleep disturbances and behavioural problems in adults with Prader–Willi syndrome

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Abstract

Background Individual with Prader–Willi syndrome (PWS) are at risk of sleep disturbances, such as excessive daytime sleepiness (EDS) and sleep apnoea, and behavioural problems. Sleep disturbances and their relationship with other variables had not been researched extensively in adults with PWS.

Method Sleep disturbances and behavioural problems were investigated in adults with genetically confirmed PWS using standardised questionnaires. Results of adults with paternal deletion (n = 45) were compared with those of adults with maternal uniparental disomy (n = 33).

Results Eleven adults with PWS (i.e. 15%) had a current sleep problem, mostly night waking problems. Twenty-six adults with PWS (i.e. 33%) suffered from severe EDS. No differences in prevalence of sleep disturbances between genetic subtypes were found. Seventeen adults with deletion (i.e. 38%) and 17 adults with maternal uniparental disomy (i.e. 52%) had behavioural problems. No significant relationships were found between sleep disturbances and behavioural problems.

Conclusions In adults with PWS, EDS is the most common type of sleep disturbance. Men and individuals with relative high body mass index are at increased risk for EDS. More research, aimed at developing a suitable screening instrument for sleep apnoea in adults with PWS, is necessary. Clinical implications of the findings are discussed.

Keywords behaviour, excessive daytime sleepiness, Prader–Willi syndrome, preventive management, questionnaire, sleep

Introduction

Prader–Willi syndrome (PWS) is characterised by infantile hypotonia, hyperphagia, intellectual disability (ID), short stature and hypogonadism (Prader et al. 1956; Holm et al. 1993; Goldstone et al. 2008; Cassidy & Driscoll 2009). PWS results from the abnormal or absent expression of the paternal copy of a maternally imprinted gene region at chromosome 15q11-q13. This can arise from four different mechanisms: a paternal deletion (70%), a maternal
uniparental disomy (mUPD) (25%), an imprinting centre defect (<5%) or an unbalanced chromosomal translocation (<1%) (Ledbetter et al. 1981; Nicholls et al. 1989; Buiting et al. 1995; Horsthemke & Buiting 2006; Goldstone et al. 2008; Cassidy & Driscoll 2009).

Temper tantrums, insistence on routine, skin-picking, obsessive traits, mood swings and stubbornness are characteristic behaviour problems often observed among individuals with PWS (Boer & Clarke 1999; Clarke et al. 2002; Holland et al. 2003; Didden et al. 2007). Also sleep disturbances, more specifically excessive daytime sleepiness (EDS) and sleep apnoea, are common in individuals with PWS (Butler & Clarke 2003). Richdale et al. (1999) performed a study on sleep disturbances in children and adults with PWS using standardised sleep questionnaires to screen for EDS, sleep apnoea and narcolepsy. They found sleep disturbances including EDS and sleep apnoea, are common in individuals with PWS (Butler et al. 2002).

Early prevalence studies in adults with PWS revealed that daytime sleepiness was observed in more than 95% of samples (Greenswag 1987; Clarke et al. 1989). Validity of outcomes of these studies is limited because no standardised sleep questionnaires were used and data on other types of sleep disturbances (e.g. difficulty falling asleep, night waking and breathing disturbances during sleep; see Vela-Bueno et al. 1984) than those indicating hypersomnia were lacking. Furthermore, in both studies diagnosis was not genetically confirmed for all participants. A decade later Richdale et al. (1999) performed a study on sleep disturbances in children and adults with PWS using standardised sleep questionnaires to screen for EDS, sleep apnoea and narcolepsy. They found sleep disturbances including EDS, snoring and night waking to be present in adults. The number of adults in their sample was rather small (i.e. n = 7).

In individuals with PWS, daytime sleepiness and poor sleep quality may be related to daytime irritability, temper tantrums and attention problems (Richdale et al. 1999; Boer 2004; O’Donoghue et al. 2005). Richdale et al. found that in children with PWS, EDS was associated with behavioural problems in all domains of the Developmental Behaviour Checklist (DBC; Einfeld & Tonge 2002). At present, studies on the relationship between sleep disturbance and behavioural problems in adults with PWS are lacking, except for Clarke et al.’s (1989) study. In their study, reports of parents showed that adults who frequently slept during the day or slept longer at night did not have more temper tantrums during the day than adults who did not show symptoms of hypersomnia. However, according to 43% of the parents impaired night time sleep in these adults was followed by irritability or temper tantrums the day after. According to these findings behavioural problems were associated with insomnia rather than with hypersomnia.

Other variables than behavioural problems may be associated with sleep disturbances in adults with PWS. In the general population obesity is related to EDS and sleep apnoea (Bixler et al. 2005; Shah & Roux 2009). Evidence supporting a positive relationship between EDS and body mass index (BMI) in individuals with PWS is mixed (Camfferman et al. 2008). Breathing disturbances during sleep, including sleep apnoea, may be exacerbated by obesity in individuals with PWS (Nixon & Brouillette 2002; Yee et al. 2007). Other variables that have previously been found to be related with sleep disturbances in adults with ID (without PWS) are gender, age, living situation, epilepsy, medication use, evening caffeine consumption, nocturnal urinary incontinence and ability to communicate (Espie & Tweedie 1991; Brylewski & Wiggs 1998). Up until now there have been no prevalence studies on different types of sleep disturbances in a large sample of adults with PWS who are genetically confirmed. Also, the relationship between sleep disturbances and other variables had not been researched extensively in adults with PWS.

This study replicates Richdale et al.’s (1999) study by using the same standardised sleep and behaviour questionnaires. It elaborates on their study by including only adults with PWS of whom the genetic subtype is confirmed. The aim of this study is threefold; it (1) investigates prevalence and nature of sleep disturbances in a Dutch cohort (n = 79) of adults with PWS across genetic subtypes; (2) explores the relationship between sleep disturbances and behavioural problems; and (3) explores associations between sleep disturbances and gender, age, BMI, living situation, medication use and behavioural problems in adults with PWS.

Method

Procedure

The study was approved by the Medical Ethics Committee of the Academic Hospital Maastricht.
and Maastricht University. Adults with PWS were approached through the Dutch Prader–Willi Parent Association and physicians specialising in people with ID. The legal representatives (mostly parents) gave their informed written consent. The individuals with PWS and their main caregivers (family and/or professional caregivers) were visited by the second author for a semi-structured interview. For each question an evaluation was made of the person who (either individual with PWS or main caregivers) would provide the most reliable information on sleeping behaviour. If the individual with PWS had moderate or severe ID and/or low verbal ability or if staff were present at night, information of main caregivers was considered more reliable than information of individuals with PWS. For most questions information was provided by main caregivers and this was more often than not in agreement with the information provided by individuals with PWS themselves. We are aware of the fact that orally administering standardised sleep questionnaires developed for the general population may threaten validity (Finlay & Lyons 2001). However, to our knowledge no self-report questionnaires for adults with ID assessing sleep disturbances have been developed so far. Information about behaviour problems was provided by main caregivers. Data on demographic information, including prescribed medication and physical conditions, were collected. The level of ID was reported by the main caregivers. Results of IQ tests were available in 52% of the cases. If no results of IQ tests were available level of ID was estimated on the basis of information (e.g. results from adaptive skills questionnaires) in participants’ files. Medical information was retrieved from physicians. Genetic testing was undertaken in case of participants who did not have a previously confirmed genetic diagnosis. DNA methylation studies on the SNURF/SNRPN locus were used to confirm the diagnosis of PWS. Cytogenetic analyses were performed to establish whether a deletion was present. Parental samples, whenever available, were used to confirm mUPD with microsatellite analysis at various loci on chromosome 15.

Participants

A total of 79 adults with PWS were included in this study, of whom 34 (43%) were male. Their mean age was 34.4 years (SD = 11.8, range = 18–65). All participants were genetically confirmed as having PWS: 45 (57%) had paternal deletion, 33 (42%) had mUPD and one (1%) participant had an imprinting centre defect. Sixty-three (80%) participants lived in an institutional residential or community residential facility while 16 (20%) participated lived at home with their parents or family. Level of ID was mild (47%, n = 37) or moderate (30%, n = 24) in most participants. Five (6%) participants had severe ID. The other participants were functioning at a borderline ID level (IQ 70–80) (10%, n = 8) or did not have ID (IQ ≥ 80) (6%, n = 5). Mean BMI (kg/m2) was 33.2 (SD = 8.0, range = 21.4–51.9). Forty-eight (61%) participants were obese (BMI ≥ 30). Twenty-six (33%) participants received (combinations of) psychotropic medication for behavioural and/or emotional problems. Six (8%) participants received medication for sleep disturbances. See Table 1 for more information on demographic characteristics and information on medication use across genetic subtypes (paternal deletion vs. mUPD).

On average, participants with deletion subtype were somewhat younger (M = 32.1, SD = 11.0, range = 18–65) than participants with mUPD (M = 37.3, SD = 12.4, range = 18–65). Results of a t-test showed that this difference approached statistical significance [t(76) = -1.98, P = 0.051]. Mean BMI scores were 33.7 (SD = 8.2, range = 21.4–51.9) for participants with deletion and 33.0 (SD = 7.7, range = 23.1–49.9) for participants with mUPD. These differences were not statistically significant [t(76) = 0.38, P = 0.71].

Materials

As part of the semi-structured interview data on settling problems, night waking and early waking were collected. Questions concerning settling, night waking and early waking were asked to determine whether current sleep problems were present according to criteria established by Wiggs & Stores (1996) and Didden et al. (2002). Frequency of occurrence of sleep problems was assessed on a 7-point Likert-type scale from ‘Never’ (1) to ‘Daily’ (7). Questions about duration were measured on a 5-point Likert-type scale from ‘A few minutes’ (1)
to ‘More than two hours’ (5). Settling problems were defined as severe if they occurred three or more nights a week, the individual took more than 1 h to fall asleep and parents or other caregivers were disturbed during this time. Settling was considered a mild problem if it occurred one or two nights a week and falling asleep took more than 30 min but less than 1 h. Night waking was defined as severe if it occurred three or more nights a week, and if the individual remained awake for more than a few minutes and disturbed parents or other caregivers during that time. Night waking was considered a mild problem if it occurred once or two nights a week and falling asleep took more than 30 min but less than 1 h. Night waking was defined as mild if it occurred once or twice a week. Participants were diagnosed with current sleep problems if they had at least one of the three types of sleep problems mentioned above and if the level of these problems was mild or severe.

Furthermore, two standardised questionnaires were included in the interview to screen for the presence of EDS and sleep apnoea. The Epworth Sleepiness Scale (ESS; Johns 1991) was used to measure the participants’ general level of daytime sleepiness. The ESS consists of eight items, indicating a variety of circumstances, which are rated on a 4-point Likert-type scale, from ‘Would never doze’ (0) to ‘High chance of dozing’ (3) (range = 0–24). ESS scores ≥ 16 are indicative of a high level of daytime sleepiness (EDS). The ESS has good internal consistency (Cronbach’s $\alpha = 0.88$) and test–retest reliability ($r = 0.82$) (Johns 1992) when administered to non-disabled individuals. ESS cut-off scores used by Richdale et al. (1999) were $7 \leq \text{ESS} < 16$ and $\text{ESS} \geq 16$ in individuals with PWS. Therefore, prevalence rates will be presented for $7 \leq \text{ESS} < 16$ and $\text{ESS} \geq 16$.

Table 1 Number and percentage of participants’ characteristics by genetic subtype (paternal deletion vs. mUPD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Del $(n = 45)$</th>
<th>mUPD $(n = 33)$</th>
<th>$\chi^2(1)$</th>
<th>$P$†</th>
</tr>
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<tbody>
<tr>
<td>Number of men</td>
<td>21 (47)</td>
<td>12 (36)</td>
<td>0.83</td>
<td>0.36</td>
</tr>
<tr>
<td>Living situation</td>
<td>33 (73)</td>
<td>29 (88)</td>
<td>2.47</td>
<td>0.12</td>
</tr>
<tr>
<td>Residential facility</td>
<td>12 (27)</td>
<td>4 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of cognitive functioning</td>
<td></td>
<td></td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>No ID (IQ ≥ 80)</td>
<td>2 (4)</td>
<td>3 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borderline (IQ 70–80)</td>
<td>6 (13)</td>
<td>2 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild ID</td>
<td>23 (51)</td>
<td>13 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate ID</td>
<td>13 (29)</td>
<td>11 (33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe ID</td>
<td>1 (2)</td>
<td>4 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication use related to</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychopathology</td>
<td>6 (13)</td>
<td>20 (61)</td>
<td>19.15</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>4 (9)</td>
<td>15 (45)</td>
<td>13.82</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1 (2)</td>
<td>6 (18)</td>
<td>0.04*</td>
<td></td>
</tr>
<tr>
<td>Mood stabilisers</td>
<td>3 (7)</td>
<td>11 (33)</td>
<td>9.19</td>
<td>0.002**</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>0</td>
<td>1 (3)</td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>3 (7)</td>
<td>3 (9)</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Melatonin</td>
<td>0</td>
<td>1 (3)</td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Miododial</td>
<td>2 (4)</td>
<td>1 (3)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Temazepam</td>
<td>0</td>
<td>1 (3)</td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

* $P < 0.05$, ** $P < 0.01$.
† In case no value for $\chi^2$ is depicted because of low cell frequencies, the $P$-value is a result of Fisher’s exact test.
Del, paternal deletion; mUPD, maternal uniparental disomy; ID, intellectual disability.
The Sleep Apnea (SA) sub-scale of the Sleep Disorders Questionnaire (SDQ; Douglass et al. 1994) consists of 12 items that are rated on a 5-point Likert-type scale, from ‘Never’ (1) to ‘Always’ (5) (range = 12–60). The SA-SDQ does not include questions about daytime sleepiness. Scores ≥36 for men and ≥32 for women are proposed as cut-off values above which sleep apnoea becomes clinically probable with satisfactory specificity (76%–81%) and sensitivity (85%–88%). Internal consistency (Cronbach’s α = 0.86) and test–retest reliability (ρ = 0.84) of the SA scale were good when administered to non-disabled individuals. A procedure for estimating a small number of missing data was as follows: a median value was calculated for each item on the basis of scores regarding that item by all respondents. Missing data were replaced by this median score.

To gather information about behavioural problems main caregivers completed a questionnaire prior to the interview. The Developmental Behaviour Checklist for Adults (DBC-A; Mohr et al. 2004) is designed to assess problematic behaviour and emotional state in adults with ID. The main caregiver rated 107 items on a 3-point Likert-type scale, as ‘Not true’ (0), ‘Sometimes or somewhat true’ (1) or ‘Often true or very true’ (2) (range = 0–321). To derive a total behaviour problem score (TBPS) all item scores were summed. TBPS ≥ 51 are proposed as cut-off with modest specificity (50%) and high sensitivity (87%) with regard to expert clinical judgement of psychiatric caseness. Furthermore, six sub-scale scores were obtained: disruptive (17 items), self-absorbed (28 items), communication disturbance (13 items), anxiety/antisocial (9 items), social relating (6 items) and depressive (10 items). Internal consistency of the total scale (Cronbach’s α = 0.95) was excellent and internal consistency of the sub-scales was substantial to good (Cronbach’s α = 0.61–0.89) (Mohr et al. 2004). Intraclass correlations for test–retest (ICC = 0.75 and ICC = 0.85) and inter-rater reliability (ICC = 0.72) were good, and concurrent validity of the DBC-A with the Aberrant Behavior Checklist (Aman & Singh 1985) (r = 0.63) and the Psychiatric Assessment Scale for Adults with Developmental Disability Checklist (Moss et al. 1998) (r = 0.61) revealed moderately positive relations (Mohr et al. 2005).

Statistical analyses

To test whether differences between genetic subtypes were statistically significant χ²-tests/Fisher’s exact tests and Independent Samples t-tests/Mann–Whitney U-tests were performed for nominal/ordinal and metric data respectively. To test the relationship between sleep disturbances and behavioural problems Kendall’s tau-b was used for ordinal data and bivariate correlation (Pearson correlation/ Kendall’s tau-b/ Spearman’s rank correlation when appropriate) for metric data. All variables that could possibly be associated with sleep disturbances in adults with PWS, i.e. gender, age, BMI, living situation, medication use related to psychopathology and TBPS, were included in a regression model to test their predictive value on the dependent sleep variables. SPSS (version 16.0) was used to analyse the data. A P-value of 0.05 or less was taken as significant for all statistical tests.

Results

Sleep disturbances

Settling problems, night waking and early waking

Percentages of participants with a current sleep problem are shown in Table 2. Eleven participants (15%, n = 75) had a current sleep problem of which night waking problems were the most common. No participants with deletion and three (9%) participants with mUPD had a problem with early waking. Differences between groups (deletion vs. mUPD) in percentage of participants with sleep problems were not statistically significant. Relationships between sleep problems and cut-off scores for EDS and sleep apnoea were weak and not statistically significant (Kendall’s tau-b range = |<0.01|–|0.09|).

Excessive daytime sleepiness

Twenty-six participants (33%) had ESS scores of 16 or higher, indicating that they suffered from EDS. The differences between groups in frequency of EDS were not statistically significant (See Table 3).

Sleep apnoea

Only three participants (4%) met criteria for sleep apnoea on the SA-SDQ (See Table 3). In both
groups (deletion and mUPD) none of the men \( (n = 33) \) met the criterion for sleep apnoea. Of the women \( (n = 45) \), two \( (8\%, n = 24) \) participants with deletion and one \( (5\%, n = 21) \) participant with mUPD met the criterion for sleep apnoea. These differences, however, were not statistically significant. SA-SDQ scores were significantly, but weakly correlated with ESS scores \( (\rho = 0.38, P = 0.001) \).

**Behavioural problems**

Thirty-five \( (44\%) \) participants, including the participant with an imprinting centre defect, had a TBPS of 51 or higher, which is indicative of clinically significant behavioural problems. Seventeen \( (38\%) \) participants with deletion and 17 \( (52\%) \) participants with mUPD had a TBPS of at least 51. This difference was not statistically significant \( [\chi^2(1) = 1.46, P = 0.23] \). Results from the Kolmogorov–Smirnov test showed that the scores on three of the six sub-scales of the DBC-A were not normally distributed. As a consequence, the Mann–Whitney \( U \)-test was used to test differences between genetic subtypes on the DBC-A sub-scales: self-absorbed, anxiety/antisocial and depressive (See Table 4). Differences between groups on DBC-A sub-scales, disruptive and self-absorbed, approached statistical significance, and on both sub-scales mean scores were higher for participants with mUPD than for participants with a deletion.

**Sleep disturbances and behavioural problems**

Information on relationships between sleep measures and the DBC-A scales is given in Table 5.
There were no significant relationships between sleep disturbances and behavioural problems.

Sleep disturbances and individual-related variables

Logistic regression analyses to predict a current sleep problem and night waking could not be performed because of low prevalence rates of those problems. However, two regression analyses (method Enter) were performed to assess to what extent (1) gender; (2) age; (3) BMI; (4) living situation; (5) medication use (related to psychopathology); and (6) behavioural problems (TBPS) predict EDS and sleep apnoea. First, analysis of ESS scores (indicating EDS) resulted in a statistically significant predictive model \(F_{6,72} = 3.52, P < 0.01, R^2 = 0.23\). Gender \(B = -3.40, P = 0.03\) and BMI \(B = 0.29, P < 0.01\) had a statistically significant impact on ESS scores. It showed that women had lower ESS scores than men and participants with higher BMI scores had higher ESS scores. Age had no statistically significant impact \(P = 0.70\).

Second, analysis of SA-SDQ scores (indicating sleep apnoea) was performed with the above mentioned variables, but without age and BMI (because these variables are included in the SA-SDQ score). This did not result in a statistically significant predictive model \(F_{4,74} = 2.25, P = 0.07, R^2 = 0.11\). Only living situation \(B = 4.64, P = 0.007\) had a statistically significant impact on SA-SDQ scores. It showed that participants living in residential facilities had higher SA-SDQ scores than participants living at home with their family. See Table 6 for results of the regression models for ESS and SA-SDQ scores.

Discussion

This study reported sleep and behaviour in a sample of adults with confirmed PWS. No differences in prevalence of sleep disturbances and behavioural problems between genetic subtypes were found. However, adults with mUPD tended to have higher scores on the disruptive and self-absorbed sub-scales of the DBC-A compared with adults with paternal deletion \(P < 0.10\). Furthermore, no relationships between sleep variables and behaviour problems were found in adults with PWS. These findings do not corroborate those of Richdale et al. (1999) who found moderate correlations between different sleep variables and all DBC scales in children and adolescents with PWS. Differences in sample characteristics (i.e. sample size, age and BMI) and lack of information about genetic diagnosis, living situation, medication use related to psychopathology and medication use related to sleep disturbances in Richdale et al.’s study, render comparisons between studies impossible.

The results show that the overall prevalence rate of a current sleep problem was relatively low (i.e. 15%). Considering the type of sleep problems, night waking problems were most often observed, i.e. in 13% of the sample. Furthermore, EDS was found
in a minority of our sample, which is in 33% of the participants. This is in contrast with other studies using parent reports and questionnaires. For example, Clarke et al. (1989) found EDS in 63% of adults with PWS. Differences in both definition and measurement of daytime sleepiness may account for the difference in prevalence rates. Greenswag (1987) and Clarke et al. did not use a standardised sleep questionnaire to measure daytime sleepiness. Richdale et al. (1999), also using the ESS to measure EDS, found a prevalence rate of 29%, which is somewhat lower than the prevalence rate in our study. The origins of EDS in PWS remain unclear (Didden et al. 2006). In this study EDS could be partly explained by gender and BMI. The model could only explain 23% of the variance. Other factors, not included in the model, such as breathing disturbances during sleep, hypothalamic dysfunction and lack of structured activities, may contribute to EDS (Nixon & Brouillette 2002; Camfferman et al. 2008; Maas et al. 2008).

Only few participants (4%) met the cut-off score for sleep apnoea. This is not in line with polysomnographic studies in individuals with PWS (Camfferman et al. 2006) in which much higher rates of sleep apnoea were found. The explanation for this difference could be twofold. First, the relatively high rate of obstructive sleep apnoea (57%) mentioned by Camfferman et al. may not be representative. Polysomnography-based information on breathing disturbances during sleep in individuals with PWS described in literature is often limited to small groups of both children and adults. These samples are highly selected in that individuals are referred because of complaints of daytime sleepiness and/or loud snoring. However, high rates of obstructive sleep apnoea have been found in a sample of unselected adolescents and adults with PWS (Yee et al. 2007). Second, experience with the SA-SDQ scale in this study leads to the conclusion that it may not be an appropriate instrument for screening of sleep apnoea in the population of adults with PWS. In this study, eight participants (four men) were previously diagnosed with sleep apnoea (confirmed by PSG or observed during surgery) and none of them met the cut-off score on the SA-SDQ. Mean SA-SDQ score of the participants previously diagnosed with sleep apnoea was 26 (range = 18–31).

Although Richdale et al. (1999) also have used this
questionnaire with individuals with PWS, the SA-SDQ is not designed for measuring sleep apnoea individuals with ID. Questions on sleeping position, snoring, audible apnoeas or awaking with a start were difficult to answer for both individuals with PWS themselves as well as their parents or caregivers. Development of cut-off scores for individuals with ID or more specifically for individuals with PWS is recommended. Specific (lower) cut-off scores on the SA-SDQ have already been developed for individuals with epilepsy (Weatherwax et al. 2003). Cut-off scores are important when it comes to referring individuals to a (sleep) clinic for additional evaluation of breathing disorders during sleep and therefore they should minimise false negatives. Treatment options are available for this serious morbidity and treatment may improve the health and the quality of life of the individuals affected.

Results of this study should be interpreted in the context of its methodological shortcomings. The first shortcoming relates to the use of informant-based screening questionnaires to assess sleep disturbances. Although not as objective as measurements like polysomnography and the Multiple Sleep Latency Test, this was the only way to collect data on sleep in a relatively large sample of adults with PWS. As mentioned before, sleep studies in PWS using polysomnography are frequently biased, because they include highly selected samples of participants. In this study there was no selection of participants based on sleep complaints. After administration of screening questionnaires, further assessment is necessary to determine whether a sleep disorder is present. Based on high scores on the standardised questionnaires five participants of this study were studied more extensively with home polygraphy in order to determine whether they should or should not be diagnosed with sleep apnoea and one of them appeared to have sleep apnoea. A second shortcoming is that we were not able to control for differences in age and use of psychotropic medication between groups. In this study, adults with mUPD were on average older and used psychotropic medication more often than those with deletion subtype. Overall age did not have an impact on ESS and SA-SDQ scores. However, medication use related to psychopathology tended to have some impact on ESS scores (See Table 6). Unfortunately, we were not able to predict the influence of age and use of psychotropic medication on settling problems, night waking and early waking, because of low rates of these sleep problems. Based on earlier reports (Clarke et al. 1989; Brylewski & Wiggs 1999) and anecdotal remarks of parents and caregivers during the interviews we suspect a relationship between night waking and behavioural and emotional problems during the day. Future research should focus on the

Table 6 Summary of regression analyses for variables predicting scores on sleep questionnaires (N = 79)

<table>
<thead>
<tr>
<th></th>
<th>ESS</th>
<th>SA-SDQ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>B</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>0.03*</td>
<td>-3.40</td>
</tr>
<tr>
<td>Age</td>
<td>0.70</td>
<td>-0.03</td>
</tr>
<tr>
<td>BMI</td>
<td>0.003**</td>
<td>0.29</td>
</tr>
<tr>
<td>Living situation†</td>
<td>0.17</td>
<td>2.95</td>
</tr>
<tr>
<td>Medication use‡(−/+)</td>
<td>0.08</td>
<td>-2.97</td>
</tr>
<tr>
<td>TBPS</td>
<td>0.09</td>
<td>-0.06</td>
</tr>
<tr>
<td>Constant term</td>
<td>0.97</td>
<td>0.14</td>
</tr>
</tbody>
</table>

* P < 0.05, ** P < 0.01.
† Family vs. residential facility.
‡ Medication use related to psychopathology.
ESS, Epworth Sleepiness Scale; SA-SDQ, Sleep Apnea sub-scale of the Sleep Disorders Questionnaire; 95% CI, 95% confidence interval of B; M, male; F, female; BMI, body mass index; TBPS, total behaviour problem score of the Developmental Behaviour Checklist for Adults; –, variables were not included in model.
relationships between sleep disturbances, such as night waking and EDS and (development of) behavioural and emotional problems in adults with mUPD.

Despite these limitations, this study has provided information about sleep disturbances and behavioural problems, which until now had not been examined with standardised questionnaires in adults with PWS across genetic subtypes.

Several clinical implications may be identified. We recommend that caregivers regularly look for sleep disturbances in adults with PWS. In our opinion, the ESS is a useful instrument that can easily be applied to determine the severity of daytime sleepiness in adults with PWS. In case of ESS scores ≥ 16 or significant changes in ESS scores further assessment of sleep disturbances and associated variables is recommended. The SA-SDQ may not be suitable for screening breathing disturbances during sleep, and other ways to screen for these sleep disorders have to be developed. Furthermore, we advise caregivers to combine looking for sleep disturbances with looking for behavioural and emotional problems. Changes in sleep patterns, e.g. difficulty falling asleep and night waking, could be a first presenting sign of psychiatric illness and should be carefully monitored, specifically in young adults with PWS who are at risk of developing psychiatric illness (Boer 2004; Dykens 2004; Soni et al. 2008). We also recommend looking for sleep disturbances when daytime behaviour becomes disorganised. Regulation of the sleep pattern could prevent worsening of behavioural and emotional problems (Wirz-Justice 2007). Once specific behavioural or psychiatric causes of the sleep disturbance have been identified, appropriate treatment can be undertaken (Costa e Silva 2006). An individual treatment plan for sleep disturbances in adults with PWS may consist of treatment of extreme obesity, treatment of sleep apnoea, sleep hygiene measures (including activities during the day, especially in weekends) (Maas et al. 2008), treatment of (night time) behaviour problems and/or psychiatric illness. Combined assessment and treatment ultimately lead to improvement of sleep quality, behaviour and daytime functioning. This could be of considerable benefit to the individuals with PWS themselves, their families and their professional caregivers.

References


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