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Incontinence and psychological symptoms in Phelan-McDermid syndrome

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Abstract

Aims: Phelan-McDermid syndrome (PMD) is a congenital syndrome caused by a deletion on chromosome 22q13.3. About 600 cases have been identified worldwide. PMD is characterized by neonatal hypotonia, moderate/severe intellectual impairment, impaired expressive language, and typical dysmorphic features. Psychological symptoms as hyperactivity, attention problems, restlessness, and stereotyped-repetitive behavior were reported. The aim of the study was to assess incontinence and associated psychological problems in PMD.

Methods: Forty-one individuals with PMD were recruited through a German support group (48.8% male; mean age 13.4 years; range, 4-55 years). Parents or caregivers completed the developmental behavior checklist (DBC), as well as the parental questionnaire: enuresis/urinary incontinence, including six questions on adaptive toileting skills.

Results: Rates of nocturnal enuresis (NE), daytime urinary incontinence, and fecal incontinence were 86%, 73%, and 79%. Rates were similar in all age groups (children, teens, adults). Constipation was present in 19%. Forty-two percent of the sample had a clinically relevant DBC score, with adults more affected than teens. Persons with NE had significantly higher "anxiety/depression" subscale scores. Toileting skills were more developed in adults than in children. Sixty-eight percent had further physical disabilities.

Conclusions: Incontinence rates in PMD are high in all age groups. However, persons with PMD can improve their toilet skills. Therefore, the assessment and treatment of incontinence in persons with PMD is recommended. Constipation does not seem to be a major problem in PMD. Due to the high prevalence rates of somatic conditions, an assessment for organic and functional incontinence is recommended.

KEYWORDS

enuresis, fecal incontinence, Phelan-McDermid syndrome, psychopathology, urinary incontinence

1 | INTRODUCTION

Phelan-McDermid syndrome (PMD) is a genetic syndrome caused by a deletion on chromosome 22q13.3.[1] Most affected persons show neonatal hypotonia, a global developmental delay, severely impaired or absent language and in some cases an accelerated growth.[1] PMD is accompanied by moderate to severe intellectual disability (ID).[2] Other typical dysmorphic features are large hands, dysplastic toenails, and reduced sweating, which bears the risk of overheating.[1] PMD is a rare syndrome, with only 600 cases known worldwide.[1] It has first been described by Phelan et al in 1988,[3] and in 2003, the haploinsufficiency of the *SHANK3* gene was identified as the genetic cause of PMD.[2] Regarding the behavioral phenotype, frequently reported symptoms are hyperactivity, impulsiveness, restlessness, repetitive behavior, sleep problems, and autistic symptoms.[1,4,5]

Nonorganic or functional incontinence is subdivided into nighttime wetting (nocturnal enuresis [NE)]), daytime wetting (daytime urinary incontinence [DUI]), and fecal incontinence (FI). According to the International Children's Continence Society (ICCS), NE, and DUI are diagnosed in children from the age of 5 years onwards after excluding organic incontinence and when wetting occurs at least 1×/month over a period of 3 months.[6] FI is diagnosed according to ROME-IV criteria in children aged 4 years and older when soiling occurs at least 1×/month after ruling out organic causes.[7] In typically developing children, the prevalence of NE, DUI, and FI are 10%, 6%, and 1% to 4%, respectively.[8]

Prevalence of incontinence in children with ID is 38% for NE, 39% for DUI, and 30% for FI in 7-year olds, and still 19% to 20% in adults.[9] Further, the higher the level of ID, the higher the prevalence of incontinence.[9]

Only few studies assessed bladder/bowel control in individuals with PMD. In an assessment of 201 persons, 24% were toilet trained in total, but the rates ranged from 18% in children up to 60% of adults.[5] Other studies reported bedwetting in 67% and constipation in 53%.[10,11]

In other genetic syndromes associated with severe ID, rates on incontinence are high in all age groups (86% in Angelman syndrome, 98% in Mowat-Wilson syndrome).[12,13]

The aim the present study was to examine incontinence, toileting skills, and associations to psychological symptoms in individuals with PMD. It is hypothesized that incontinence rates are high in all age groups (children, adolescents, adults), but that adaptive toileting skills are better established in older individuals with PMD.

2 | MATERIALS AND METHODS

Participants were recruited through the PMD support group "Phelan-Mc-Dermid-Gesellschaft e.V.," with members from Germany, Austria, and Switzerland. Packages including questionnaires, an information sheet, and return envelopes were sent to the chairs of the support group, who forwarded them to all member families (n = 100) in January 2017. Following informed consent, parents or caregivers completed the questionnaires and send them back anonymously. The study was approved by the local ethics committee.

The packages comprised the "parental questionnaire: enuresis/urinary incontinence (PQ-EnU),"[14] "encopresis questionnaire—screening version,"[15] and six additional questions about adaptive toileting skills. The PQ-EnU is a valid and reliable tool to assess incontinence and was used in studies assessing incontinence in other genetic syndromes.[12,13] NE and DUI were diagnosed according to the ICCS criteria for frequency and duration in persons 5 years or older when wetting occurs ≥1 × /month.[6] FI was diagnosed according to ROME-IV criteria in children 4 years or older when soiling occurs ≥1×/month.[7]

Psychological symptoms were assessed by the German version of the developmental behavior checklist (DBC)[16] either in the parental version (DBC-P) for children/adolescents (<18 years), or in the adult version (DBC-A). The DBC-P includes five subscales "disruptive/antisocial" (DA), "self-absorbed," "communication disturbance," "anxiety" (A), and "social relating" (SR), next to the "total behavior problem score" (TBPS). The DBC-A consists of the same subscales except that the fourth scale is named "anxiety/depression." A TBPS above 46 in the DBC-P and above 51 in the DBC-A are considered as clinically relevant.[16,17] In the present study, the DBC-P and the DBC-A questionnaires were evaluated with the German norms for severe ID.[16,17]

Statistical analyses were performed with IBM SPSS Statistics 23, including descriptive statistics and nonparametric tests (χ^2 tests, Fisher's exact tests, Kruskal-Wallis test) for categorical data and parametric tests (multivariate analysis of variance [MANOVA], univariate analysis of variance (ANOVA), the Student *t* tests, the Welch tests) for interval data. Results were considered significant at $P < .05$.

3 | RESULTS

A total of 47 incontinence and 42 DBC questionnaires out of 100 sent out packages were returned. Four children were below the age of 4 years and were excluded from the analysis. The DBC could not be evaluated in case of cases, as the questionnaire was incomplete or not sent back.

Age ranged from 4.3 to 55.3 years, mean age was 13.4 years (SD = 10.9). Age was not reported in two cases. Total, 48.7% of the sample were male and 92.1% had at

least one subtype of incontinence; 85.7% had NE, 73.0% had DUI, and 78.9% had FI. Incontinence did not differ between males and females (Table 1). A total of 68.4% had a somatic condition, the most common was muscular (36.6%), neurological (19.5%), and conditions of the genitourinary tract (14.6%) and 50% received medication, including anticonvulsants, neuroleptics, and laxatives.

The sample was subdivided into three age groups (children, teens, adults, see Table 2). Incontinence was were high in all age groups and did not differ significantly between the groups. In children, 91% had NE, 83% had DUI, and 95% had FI. Adolescents had high rates of NE (80%), but lower rates of DUI (40%) and FI (50%). In adults, rates were slightly lower compared to children, but the difference did not reach statistical significance. Rates of constipation were lower: 22% of children, 20% of adolescents and none of the adults. There was a significant difference in psychopathology, as none of the adolescents, 42% of the children and all adults had a clinically relevant DBC score (Table 2). For group comparisons of the DBC subscales, mean item scores (MIS) were calculated. Significant differences were found for the subscale "disruptive/antisocial" with higher scores for adults than for teens, and for the subscale "communication disturbance," where post hoc tests did not show clear differences.

To assess the association of incontinence subtype and psychopathology, MANOVA's with the MIS of the five subscales as dependent variables and the between-factors NE, DUI, and FI (yes/no) were calculated. Significant differences were found for individuals with NE ($F[5; 23] = 3.14$; $\boldsymbol{P = .026}$*), but not for DUI ($F[5; 23] = 0.640$; $P = .67$) or FI [$F(5; 25] = 1.69$; $P = .174$). Regarding the ANOVA, persons with NE had significantly higher MIS in the subscale "anxiety/depression" ($\boldsymbol{P = .047}$*) and lower MIS in "social relations" ($\boldsymbol{P = .022}$*).

Table 3 gives a descriptive overview of adaptive toileting skills and NE, DUI, and FI symptoms. In general, toileting skills are reported more often in adolescents and adults than in children. But still, the majority wears diapers and needs help with toileting.

TABLE 1 Descriptive data of the sample including sex differences

	Total (N = 41)	Male (N = 20)	Female (N = 21)	Significance[a]
Mean age in years (SD)	13.4 (10.9)	16.7 (14.0)	10.3 (5.3)	ns[b]
Incontinence overall, % (n)	92.1 (35/38)	94.4 (17/18)	90.0 (18/20)	ns
Nocturnal enuresis, % (n)	85.7 (30/35)	82.4 (14/17)	88.9 (16/18)	ns
Daytime urinary incontinence, % (n)	73.0 (27/37)	73.7 (14/19)	72.2 (13/18)	ns
Fecal incontinence, % (n)	78.9 (30/38)	84.2 (16/19)	73.7 (14/19)	ns
Constipation, % (n)	19.4 (7/36)	26.7 (4/15)	14.3 (3/21)	ns
Clinical DBC[c] % (n)	42.4 (14/33)	57.1 (8/14)	31.6 (6/19)	ns
Somatic conditions, % (n)	68.4 (26/38)			
Cardiovascular	9.8 (4/41)	5.0 (1/20)	14.3 (3/21)	ns
Endocrinological	0 (0/41)	0 (0/20)	0 (0/21)	…
ENT	2.4 (1/41)	5.0 (1/20)	0 (0/21)	ns
Gastrointestinal tract	7.3 (3/41)	10.0 (2/20)	4.8 (1/21)	ns
Genitourinary tract	14.6 (6/41)	10.0 (2/20)	19.0 (4/21)	ns
Immune system	7.3 (3/41)	10.0 (2/20)	4.8 (1/21)	ns
Muscular	36.6 (15/41)	35.0 (7/20)	38.1 (8/21)	ns[e]
Neurological	19.5 (8/41)	30.0 (6/20)	9.5 (2/21)	ns
Sensory organs	4.9 (2/41)	10.0 (2/20)	0 (0/21)	ns
Skeletal	2.4 (1/41)	5.0 (1/20)	0 (0/21)	ns
Skin	2.4 (1/41)	0 (0/20)	4.8 (1/21)	ns
Medication, % (n)[d]	50.0 (20/40)	65 (13/20)	35 (7/20)	ns[e]

Note: ns, $P \geq .05$.

Abbreviations: DBC, developmental behavior checklist; ENT, Ear, nose, and throat; ns, not significant; TBPS, total behavior problem score.

[a]Fisher's Exact test if not otherwise labeled; *$P < .05$; **$P < .01$; ***$P < .001$.

[b]The Student t test.

[c]Clinical DBC is defined as a TBPS >46 in the DBC-P or a TBPS >51 in the DBC-A.

[d]Most frequent medication: anticonvulsants (n = 10), neuroleptics (n = 4), laxatives (n = 3).

[e]χ^2 test.

TABLE 2 Incontinence, constipation, and clinical DBC over the age groups

	Total N = 41	Children (C) (4-12 y), N = 28	Teens (T) (13-17 y), N = 5	Adults (A) (≥18 y), N = 8	Significance[a]
Mean age in years (SD)	13.4 (10.9)	8.0 (2.3)	14.8 (1.3)	31.3 (13.1)	
Incontinence overall, % (n)	92.1 (35/38)	96.2 (25/26)	100 (5/5)	71.4 (5/7)	ns
Nocturnal enuresis, % (n)	85.7 (30/35)	91.3 (21/23)	80.0 (4/5)	71.4 (5/7)	ns
Daytime urinary incontinence, % (n)	73.0 (27/37)	83.3 (20/24)	40.0 (2/5)	62.5 (5/8)	ns
Fecal incontinence %, (n)	78.9 (30/38)	85.2 (23/27)	50.0 (2/4)	71.4 (5/7)	ns
Constipation, % (n)	19.4 (7/36)	22.2 (6/27)	20.0 (1/5)	0 (0/4)	ns
Clinical DBC[b], % (n)	42.4 (14/33)	42.3 (11/26)	0 (0/4)	100 (3/3)	**.03*** (A >T)
DBC total MIS (SD)	0.48 (0.20)	0.47 (0.21)	0.38 (0.08)	0.68 (0.12)	ns
DBC subscales MIS (SD)					
Disruptive/antisocial	0.47 (0.27)	0.46 (0.26)	0.31 (0.18)	0.83 (0.18)	**.029*** (A >T)
Self-absorbed	0.63 (0.30)	0.63 (0.32)	0.63 (0.18)	0.65 (0.34)	ns
Communication disturbance	0.41 (0.35)	0.38 (0.29)	0.21 (0.04)	0.98 (0.64)	**.017**[c]
Anxiety/(depression)[d]	0.41 (0.28)	0.43 (0.27)	0.19 (0.14)	0.51 (0.39)	ns
Social relating	0.39 (0.28)	0.34 (0.27)	0.48 (0.13)	0.64 (0.44)	ns

Note: ns, $P \geq .05$.

Abbreviations: ANOVA, analysis of variance; DBC, developmental behavior checklist; MIS, mean item score; ns, not significant; TBPS, total behavior problem score.

[a]Fisher's exact tests in nonparametric data, ANOVAs in interval data.

[b]Clinical DBC is defined as a TBPS >46 in the DBC-P or a TBPS >51 in the DBC-A.

[c]Kruskal-Wallis exact test due to missing normal distribution of the variable.

[d]In the DBC-A the subscale is named "anxiety/depression."

*$P < .05$

Table 4 describes voiding and stool habits. Of the 14 persons who do not wear diapers the whole day, micturition frequency (4-7×/day) and the time between voids (3-4 hours) is normal in most cases. Sixty percent of children and teens must be sent to the toilet and do not take enough time for voiding, which is not found in adults. Most of the individuals have regular bowel movements (1×/day or every other day), with mostly soft stools, and no history of retention or painful bowel movements.

4 | DISCUSSION

The present study is the first to specifically analyze incontinence, stool and voiding habits, and their association with psychological symptoms in a sample of children, adolescents, and adults with PMD syndrome.

Overall incontinence was high in all age groups. Although rates were lower in adults than in children, the difference was not statistically significant, probably due to small sample sizes. This is in contrast to former findings, as there was a difference between age groups in the study of Sarasua et al, in which 82% of children, 68% of adolescents, and 40% of adults were not toilet trained.[5] This can be explained by definition terms, as "toilet trained" does not necessarily mean "continent." In the present study wetting/soiling was defined when occurring at least 1×/month.[6,7] Unfortunately, Sarasua et al did not report how they defined "toilet trained." It could include persons who learned using the toilet to void or defecate but still have "accidents," which would meet the ICCS or ROME-IV criteria of incontinence. When comparing the rates of how many go to the toilet themselves in the present study, the rates are similar in both studies.

The presence of ID is perhaps a major contributory factor towards the high prevalence of incontinence in PMD. When comparing present incontinence rates to those of other genetic syndromes associated with severe ID, similar findings can be reported (86% in Angelman, 98% in Mowat-Wilson syndrome.[12,13] In severe ID, the attainment of skills, eg, language, daily tasks, and social interaction is limited and affected persons need ongoing assistance through their whole life. One can imagine that these persons have problems to perceive signals of a full bladder or bowel, to associate it with emptying it into the toilet and to communicate the need to go to the bathroom. The limited possibility to learn new skills

TABLE 3 Adaptive toileting skills and incontinence symptoms reported by caregivers in all age groups

	Total	Children (4-12 y)	Teens (13-17 y)	Adults (≥18 y)	Significance[b]
Adaptive toileting skills (total N)	41	28	5	8	···
Does he/she wear diapers during the day?[a] (%)	89.7	85.7	100	100	ns
Does he/she use the toilet to pass urine? (%)	32.4	24.0	50.0	50.0	ns
Does he/she use the toilet to pass stools? (%)	32.4	23.1	50.0	57.1	ns
Does your child go to the toilet himself/herself if he/she needs to?	37.5	28.5	75.0	50.0	.064
Does he/she tell you when he/she has to go to the toilet? (%)	18.4	7.4	40.0	50.0	**.018***
Does he/she need help when he/she goes to the toilet? (%)	91.2	95.5	100	71.4	ns
Nocturnal enuresis (total N)	30	21	4	5	···
How often does he/she wet the bed?					
Every night	86.7	90.5	75.0	80.0	ns
2×/wk or more	6.7	4.8	0	20.0	
1×/mo or more	6.7	4.8	25.0	0	
Has he/she ever been dry during the night for more than 6 mo? (%)	62.1	66.7	25.0	75.0	ns
Does he/she wake up to go to the toilet? (%)	6.7	9.5	0	0	ns
Is he/she a deep sleeper, ie, difficult to wake up? (%)	12.0	18.8	0	0	ns
Daytime urinary incontinence (total N)	27	20	2	5	···
How often does he/she wet himself/herself during the day?					
Every day	88.9	90.0	100	80.0	ns
2×/wk or more	11.1	10.0	0	20.0	
1×/mo or more	0	0	0	0	
How many times a day does he/she wet?					
Once or twice	16.7	17.6	0	20.0	ns
3-4 times	8.3	0	0	40.0	
5-6 times	41.7	41.2	50.0	40.0	
More	33.3	41.2	50.0	0	
Does he/she notice when he/she wets?	22.7	18.8	0	40.0	ns
Fecal incontinence (total N)	30	23	2	5	···
How many times a week does he/she soil?					
Every day	76.7	78.3	50.0	80.0	ns
2×/wk or more	20.0	17.4	50.0	20.0	
1×/mo or more	3.3	4.3	0	0	
How often does he/she soil per day?					
Once or twice	72.4	68.2	100.0	80.0	ns
3-4 times	20.7	27.3	0	0	
5-6 times	6.9	4.5	0	20.0	
How large are the stool masses?					
Small amounts	6.9	4.5	0	20.0	ns
Moderate amounts	65.5	63.6	100.0	60.0	
Large amounts	27.6	31.8	0	20.0	
What is the consistency of his/her stool?					
Hard	3.3	4.3	0	0	ns
Soft	60.0	60.9	50.0	60.0	
Watery	10.0	13.0	0	0	
Varying consistency	26.7	21.7	50.0	40.0	
Does he/she soil during sleep/the night?	42.3	35.0	0	80.0	ns

Abbreviation: ns, not significant.

[a]Includes all persons that wear diapers always or occasionally.

[b]Fisher's exact tests.

may lead to higher incontinence rates in individuals with PMD.

There are also differences in specific subtypes of incontinence between different syndromes. In PMD, NE is the most frequent type (86%), whereas in other syndromes, eg, Mowat-Wilson syndrome, FI was the most common type.[12] This implicates that further aspects aside from ID, eg, neurobiological causes, may play a contributing role towards incontinence. The rate of NE in the present study is higher than in the study of Bro et al, in which 67% reported bedwetting.[10] In the present study, NE was diagnosed according to ICCS criteria[6] with an incontinence-specific questionnaire, so less (true) cases were probably missed.

NE is caused by maturational deficits in the central nervous system (CNS) which lead to an impaired arousal at night or to an inhibition deficit of the micturition reflex during sleep in the pontine micturition center of

TABLE 4 Voiding and stool habits in individuals with PMD

	Total	Children + teens (4-17 y)	Adults (≥18 y)
Voiding habits[a] (total N)	**14**	**10**	**4**
How often does your child pass urine during the day?			
1-3×	14.3	20.0	0
4-7×	85.7	80.0	100
>7×	0	0	0
How long can your child manage without going to the toilet (during shopping, car trips, etc)?, h			
0-1	6.7	0	16.7
1-2	33.3	33.3	33.3
3-4	46.7	55.6	33.3
5 h or more	13.3	11.1	16.7
Does your child have to push to begin urinating?	25.0	33.3	0
When your child needs to pass urine, does he/she have to rush to the toilet immediately?	23.1	22.2	25.0
Does your child try to postpone passing urine by crossing his/her legs, squatting, etc?	16.7	20.0	0
Does your child wet him/herself while he/she is rushing to pass urine?	0	0	0
Does your child have to rush to the bathroom to pass urine even if he/she went a short time ago?	0	0	0
Do you have to send your child to the toilet?	42.9	60.0	0
When your child voids, is the stream interrupted?	30.8	40.0	0
Does your child hurry and not take enough time for voiding?	46.2	60.0	0
Does your child feel a sudden urge to go to the toilet?	18.2	12.5	33.3
Does urine dribble constantly?	0	0	0
Does your child wet his/her clothes immediately after having gone to the toilet?	7.1	9.1	0
Over the past 4 wk, did your child have a urinary tract infection?	0	0	0
	Total	**Children + teens (4-17 y)**	**Adults (≥18 y)**
Stool habits (total N)	**39**	**32**	**7**
How often does your child have bowel movements?			
Every day	84.6	84.4	85.7
Every other day	12.8	12.5	14.3
2×/wk	2.6	3.1	0
Less than 2×/wk	0	0	0
What is the consistency of your child's stool?			
Hard	5.0	6.1	0
Soft	60.0	63.6	42.9
Watery	5.0	6.1	0
Varying consistency	30.0	24.2	57.1
How large are the stool masses in the toilet?			
Small	0	0	0
Medium	62.2	63.3	57.1
Large	37.8	36.7	42.9
Is defecation painful for your child?	5.3	6.3	0
Does your child withhold stool?			
Every day	6.3	6.9	0
≥1×/wk	9.4	10.3	0
≥1×/mo	9.4	10.3	0
Never	75.0	72.4	100
Does your child have stomach or abdominal pains?	6.1	6.9	0

Abbreviation: PMD, Phelan-McDermid syndrome.

[a]Only in children that never or occasionally wear diapers.

the brainstem.[18] CNS anomalies were found in a subgroup of PMD conducting brain imaging studies in different regions, eg, the corpus callosum, left temporal lobe, or amygdala.[4] Unfortunately, it was not assessed yet, which brain regions or neuronal networks that are involved in bladder and bowel control are affected in PMD. Further investigation including brain imaging assessments is recommended.

Maturational deficits, caused by genetic causes of ID, lead to a delayed achievement of bladder and bowel control and incontinence. The haploinsufficiency of the *SHANK3* gene reduces the production of the SHANK3 protein, which is involved in the formation and maturation of dendritic spines.[2,19] Loss of *SHANK3* affects neurotransmission, especially, it reduces the corticostriatal connectivity and the number of corticostriatal synapses.[19] The reduced neuronal connectivity may impair signal transmission, eg, which is important for bladder/bowel emptying, and therefore causes incontinent episodes.

SHANK3 knockout mice show impaired social, repetitive, and self-injurious behavior.[1,19] In humans, deletions of the *SHANK3* gene are discussed as a genetic cause of autism spectrum disorder (ASD), which is very common in persons with PMD.[1,11,19] It is known that persons with ASD are at a much higher risk to have incontinence,[20] which may contribute to incontinence in PMD, too.

The deletion size in PMD is significantly correlated to adaptive skills, developmental delay, growth, and hypotonia.[2,5] It has not been assessed so far if deletion size is associated with the development of bladder and bowel control. More research could provide further information on genetic associations with incontinence.

Another difference between PMD and other syndromes with severe ID is the low rate of constipation in the present study (19%). In contrast, in Angelman syndrome constipation was found in 46%.[12,13] In other publications based on medical records, constipation rates in PMD were higher (41%-53%).[5,11] Regarding ROME-IV criteria of constipation in the present study, symptoms are not that frequent: 2.6% have bowel movements twice/week or less, only 5% report hard stools, 5.3% have a painful defecation, and 6.3% withhold stool. These reports support the low constipation rate, as parental underreporting of symptoms can be excluded. Similar low constipation rates were found in children with Fragile-X-syndrome that were clinically examined.[21] The implication is: for patients with PMD, as well as for Fragile-X-syndrome, the low frequency of constipation is possibly syndrome-specific. Genetic, biological, or epigenetic factors could play a major role here. Another explanation of the divergence in rates might be that constipation in the present study is already treated (as laxatives are used as medication) and that parents pay attention to regular bowel movements and a balanced diet. Further longitudinal studies including clinical examination would clarify this specific finding.

Another risk factor for incontinence is renal and genitourinary tract anomalies. Individuals with PMD have higher rates (urinary tract infections, renal anomalies, vesicouretheral reflux) (15%) than in the general population (0.3%).[22] A clinical examination in children with incontinence is necessary to exclude organic forms and is also possible and recommended in persons with special needs, ie, genetic syndromes.[23] Due to the questionnaire design in this study, a clinical examination was not feasible. Therefore, some affected persons had possibly organic incontinence.

When looking at voiding habits in those who do not wear diapers all day (=34.1%), most persons have a regular voiding frequency (4-7×/day). Similar results arise when looking at stool habits: the majority has daily bowel movements (85%) and soft stools (60%). This implicates that it is possible to train with individuals with PMD to have a normal voiding and stool behavior. Important is that parents/caregivers send him/her to the toilet on a regular basis and pay attention that he/she takes enough time for voiding. These results are in line with Philippe et al, who found that five of eight children with PMD gained daytime bladder control at the age of 4 to 6 years, and two gained nighttime continence at the age 4 to 8 years.[4] Therefore, it is possible, that persons with PMD can be toilet trained, even though in some, incontinent episodes still may occur.

Forty-two percent had clinically relevant psychological symptoms. Adults were more affected than teens, but this must be interpreted cautiously due to small sample sizes. Other studies report a similar or even higher prevalence of impulsivity (47%), aggression (28%-47%), hyperactivity (65%), ASD (31%-69%), or stereotyped behavior (79%).[4,5,11] The highest MIS was found for the subscale "self-absorbed," which includes specific items related to severe ID (eg, "stares at lights or spinning objects," "..in his/her own world").[16] Adults had the highest scores regarding DA symptoms and communication problems, which could represent the behavioral phenotype of PMD.

Further, persons with PMD and NE have higher scores on the DA scale, but lower scores on the social relating scale. In typically developing children, NE is associated with internalizing symptoms[24] developing as a consequence to incontinence, as it affects self-esteem and decrease quality of life. It is unclear whether NE has an influence on mood in persons with PMD, or if the questionnaire was completed by parents/caregivers, who

assumed that their children must suffer from incontinence. Lower scores in the scale "social relating" imply less autistic-specific symptoms[16] which stands in contrast to the presumed connection of autism and incontinence. A possible explanation may be that neuroleptics decrease aggression and impulsivity and hence improve social behavior on the one hand; on the other hand neuroleptics, especially clozapine, induce nighttime incontinence as a side effect.[25] In the present study, four persons received antipsychotic medication, two of them had NE. The sample sizes are too small to calculate any associations. The relations between SR, incontinence, and antipsychotic medication should be assessed in future studies with larger samples.

4.1 | Clinical implications

In general, rates of incontinence were high in all age groups. But, training and improvement of toileting skills are possible, so that a normal voiding and stool behavior can be achieved. The findings from this study further suggest that incontinence should be added as a core clinical feature within the behavioral phenotype of people with PMD. However, support and assistance from caregivers are necessary. In all patients with PMD and incontinence, a medical examination should be conducted including ultrasound, a 48-hour bladder diary and uroflowmetry to exclude organic forms of incontinence according to ICCS guidelines.[6] All examinations can be applied to individuals with special needs, as well.[23] Psychological symptoms are present in many individuals, which may complicate treatment and should be diagnosed and treated in all individuals. This study also demonstrated that the German version of the DBC serves as a practical screening tool for psychological symptoms in persons with ID within German-speaking countries.

4.2 | Strengths and limitations

Strength of the study is the systematic assessment of all types of incontinence with a validated questionnaire according to current guidelines. Limitations are the small sample, and that data were only assessed by parental reports.

5 | CONCLUSIONS

Incontinence rates in PMD are high in all age groups but an improvement of toileting skills is possible. We recommend assessment and treatment of incontinence in all individuals with PMD. Constipation does not seem to be a major problem in PMD. Due to the high prevalence rates of somatic conditions, assessment, and treatment of incontinence in persons with PMD should be part of the diagnostic process.

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