Research in Developmental Disabilities 62 (2017) 230–237

Contents lists available at ScienceDirect

Research in Developmental Disabilities

Incontinence and psychological symptoms in individuals with Mowat-Wilson Syndrome

Justine Niemczyk[a,*], Stewart Einfeld[b], David Mowat[c], Monika Equit[d], Catharina Wagner[a], Leopold Curfs[e], Alexander von Gontard[a]

[a] Department of Child and Adolescent Psychiatry, Saarland University Hospital, Homburg 66421, Germany
[b] Centre for Disability Research and Policy, Brain and Mind Research Institute, University of Sydney, Sydney, NSW, Australia
[c] Department of Medical Genetics, Sydney Children's Hospital, NSW, Australia
[d] Department of Clinical Psychology and Psychotherapy, Saarland University, Saarbruecken, Germany
[e] Department of Clinical Genetics, Governor Kremers Centre, Maastricht University Medical Centre, Maastricht, The Netherlands

ARTICLE INFO

Article history:
Received 21 July 2016
Received in revised form 3 November 2016
Accepted 4 January 2017
Available online 13 January 2017
Number of reviews completed is 2

Keywords:
Mowat-Wilson Syndrome
Urinary incontinence
Fecal incontinence
Enuresis
Psychopathology

ABSTRACT

Background: Mowat-Wilson Syndrome (MWS) is caused by deletion/mutation of the *ZEB2* gene on chromosome 2q22. MWS is characterized by a distinctive facial appearance, severe intellectual disability and other anomalies, e.g. seizures and/or Hirschsprung disease (HSCR). Most individuals have a sociable demeanor, but one third show psychological problems.
Aims: The aim was to investigate incontinence and psychological problems in MWS.
Methods and procedures: 26 children (4–12 years), 13 teens (13–17 years) and 8 adults (>18 years) were recruited through a MWS support group. The Parental Questionnaire: Enuresis/Urinary Incontinence, as well as the Developmental Behaviour Checklist (DBC) were completed by parents or care-givers.
Outcomes and results: 97.7% of persons with MWS had incontinence (nocturnal enuresis 74.4%; daytime urinary incontinence 76.2%; fecal incontinence 81.4%). Incontinence remained high over age groups (children 95.8%, teens 100%, adults 100%). 46.2% of children, 25% of teens and 37.5% of adults exceeded the clinical cut-off on the DBC. The ability to use the toilet for micturition improved with age.
Conclusions and implications: MWS incontinence rates are very high. All had physical disabilities including anomalies of the genitourinary and gastrointestinal tract. Due to the high prevalence rates, a screening for incontinence and psychological problems in MWS is recommended.

What this paper adds?

This study is the first assessment of incontinence in a group of children, teens and adults with MWS. Results show very high prevalence of incontinence, with no significant differences between age groups. Although incontinence rates remain high, some adaptive toileting skills are present in adults with MWS. Due to physical disabilities both, functional and organic incontinence could be present.

* Corresponding author.
E-mail address: justine.niemczyk@uks.eu (J. Niemczyk).

http://dx.doi.org/10.1016/j.ridd.2017.01.006
0891-4222/

1. Introduction

1.1. Mowat-Wilson Syndrome

Mowat-Wilson Syndrome (MWS) is a congenital syndrome caused by a deletion or mutation of the *ZEB2* gene on chromosome 2q22 (Mowat & Wilson, 2010, Chapter 35). It was first described by Mowat et al. (1998) in six individuals with symptoms of severe intellectual disability (ID), microcephaly, short stature and Hirschsprung disease (HSCR) (Mowat et al., 1998). Further characteristics of MWS are typical facial features (prominent nasal tip and chin, cupped ears with upturned lobes, deep-set eyes, hypertelorism, broad medially sparse eyebrows), severe developmental delay, seizures, constipation and a happy, social demeanor (Adam et al., 2006; Mowat & Wilson, 2010, Chapter 35). Prevalence is estimated at 1: 50,000–70,000 (Mowat & Wilson, 2010, Chapter 35).

1.2. Behavioral phenotype of Mowat-Wilson Syndrome

The behavioral phenotype in MWS was examined by Evans et al. in a sample on 61 individuals, who found less depressive or mood problems, more oral (as chewing objects or grinding teeth) and stereotyped behaviours and an underreaction to pain in comparison to a group of non-syndromatic persons with ID (Evans et al., 2012). Further descriptions of MWS point out the happy demeanor, sociability and frequent laughter, but also self-injuring and hyperactive behavior (Adam, Justice, Bean, & Fernhoff, 2008; Mowat & Wilson, 2010, Chapter 35). Sleep disturbances with an association to psychological problems are also found in MWS (Evans, Mowat, Wilson, & Einfeld, 2016). Intelligence in MWS is mostly in the range of severe ID (Evans et al., 2012; Garavelli et al., 2009).

1.3. Incontinence

Functional incontinence (including nocturnal enuresis (NE), daytime urinary incontinence (DUI) or fecal incontinence (FI)) is a common disorder affecting about 1–10% of typically developing children and decreasing to <1% in adolescence and adulthood (Franco, Austin, Bauer, von Gontard, & Homsy, 2015). In individuals with ID, incontinence rates are much higher (approx. 30–40%), and are associated with the level of ID (von Wendt, Simila, Niskanen, & Jarvelin, 1990). In a population-based sample, 33–38% of 7-year-old children with severe ID had some subtype of incontinence, and at the age of 20 years, 19–24% of individuals with severe ID still had incontinence problems (von Wendt et al., 1990).

1.4. Incontinence in Mowat-Wilson Syndrome

Incontinence has not been systematically examined in MWS. In a report on 12 cases with MWS aged 0–23 years, 3 of the 8 individuals who were older than 4 years were not toilet trained, one was in the process of toilet training and 3 were continent (Adam et al., 2006). HSCR is a condition often associated with constipation and FI and is found in approximately 45% of MWS patients (Coyle & Puri, 2015). In a review of published cases, constipation was reported in 30%, genitourinary and renal anomalies in 52% (Garavelli et al., 2009).

1.5. Aim of the study

The aim of this study was to examine incontinence subtypes, associated conditions (constipation, lower urinary tract symptoms (LUTS), anomalies of the genitourinary and gastrointestinal tract), adaptive toileting skills and behavioral symptoms in different age groups of individuals with MWS.

2. Material and methods

2.1. Procedure

Packages with questionnaires were sent to all member families of the German Mowat-Wilson Syndrome support group "Mowat-Wilson Deutschland". As it comprises only 10 families, the study was also announced on the homepage of the International Mowat-Wilson Foundation. Questionnaires in four languages were provided (English, German, French, Italian), which could be requested online by interested families. Following informed consent, parents or caregivers were asked to complete the questionnaires and send them back. Questionnaires were sent out and received over 28 months (June 2013–October 2015).

2.2. Instruments

Incontinence was assessed by the "Parental Questionnaire: Enuresis/Urinary Incontinence" (von Gontard, 2012b), "Encopresis Questionnaire – Screening Version" (von Gontard, 2012a). Six questions about adaptive toileting skills were added

to the questionnaire. LUTS were assessed by the German version of the "International-Consultation-on-Incontinence-Questionnaire – Pediatric Lower Urinary Tract Symptom" (ICIQ-CLUTS) (De Gennaro et al., 2010). The 10 questions of the ICIQ-CLUTS build a LUTS-score with clinically relevant scores over 13. According to the International Children's Continence society (ICCS), NE and DUI were diagnosed in persons older than 5 years when wetting occurs at least once per month (Austin et al., 2015). According to DSM-5, FI was diagnosed from the age of 4 years when soiling occurs at least once per month (American Psychiatric Association (APA), 2013).

Psychological problems were assessed by the Developmental Behaviour Checklist (DBC) (Einfeld & Tonge, 2002; Mohr, Tonge, Einfeld & Taffe, 2011). The DBC is composed of five subscales ("Disruptive/Antisocial", "Self-Absorbed", "Communication Disturbance", "Anxiety" and "Social Relating") that add up to the Total Behavior Problem Score (TBPS). Parents or caregivers filled out either the parental version of the DBC (DBC-P) for children or adolescents, or the adult version (DBC-A) for adults. The DBC-A has an additional scale "Depression".

Clinically relevant scores are defined as a TBPS > 46 in the DBC-P and as a TBPS > 51 in the DBC-A, respectively (Einfeld & Tonge, 2002; Mohr et al., 2011). In addition, DBC-P/A Total scores can be expressed in percentiles according to norms for children and adults with mild, moderate and severe intellectual disability, that are available for both, DBC-P and DBC-A (Einfeld & Tonge, 2002; Mohr et al., 2011). Mean Item scores are provided for the subscales. The DBC has a high reliability (DBC-P: r = 0.80–0.83; DBC-A: r = –0.69–0.72) and a significant concurrent validity with questionnaires and expert rating (DBC-P: r = 0.72–0.86; DBC-A: r = 0.52–0.63) (Einfeld & Tonge, 2002; Mohr et al., 2011). DBC-P and DBC-A questionnaires were evaluated according to the norms of severe intellectual disability in the present sample.

The study was approved by the local ethics committee.

2.3. Statistical analysis

Statistical analyses performed by IBM SPSS Statistics 23 included descriptive statistics, and nonparametric tests ($\chi 2$–tests, Fisher's Exact tests) for categorical data and parametric tests (univariate ANOVA, Student *t*-tests, Welch tests) for parametric data. Results were considered significant at a *p*-value < 0.05.

3. Results

Packages were sent to 10 German families with a member affected by MWS. Further, 110 online requests of questionnaires were received from 18 different countries, but most from the USA, Australia and the UK. 48 questionnaires were completed and sent back. Due to an age of less than four years, one participant was excluded. The majority of questionnaires was completed by the mother (91.5%), in 6.4% by the father and in 2.1% (n = 1) the person was unknown.

3.1. Descriptive data

Descriptive data are outlined in Table 1. Mean age of the sample was 13.0 years (range 4–33 years) with a nearly equal gender distribution (20 males, 27 females). Medical conditions were frequent with HSCR reported in 38.3% and genitourinary/renal anomalies in 36.2%. A DBC score in the clinical range was found in 39.1%.

3.2. Incontinence and DBC data in the total sample

Incontinence data are available for 43 persons. All but one person were affected by incontinence (97.5%). Rates of FI (82.1%) were higher than of NE (72.5%) or DUI (74.4%) in the total sample. The mean LUTS score was 5.2 (SD = 2.1, range 0–8), but was only calculated in persons who did not wear a diaper all day (n = 6). There were neither significant gender differences in the clinical DBC scores (Chi^2=0.120; df = 1; p=0.729) nor in the rates of incontinence (Fisher's Exact test; p=0.419).

3.3. Incontinence and DBC data over age groups

The sample was subdivided into three age groups (4–12 years, 13–17 years, ≥18 years). Table 2 shows rates of incontinence, constipation, clinical DBC scores and mean item scores of the DBC subscales over the age groups. Rates of incontinence did not change significantly over age but remained at a high level. Also, the age groups did not differ regarding clinical DBC scores. The rates of constipation increased significantly from 12% in childhood to 54.5% in adolescence and 50% in adulthood, respectively.

The analysis of subtypes of incontinence (NE (n = 31), DUI (n = 31), FI (n = 34)) and clinical DBC scores (n = 16) revealed no significant associations (Fisher's Exact tests; p = 0.481 for NE; p = 1.00 for DUI; p = 0.688 for FI). Regarding mean item scores of the DBC subscales, there was a significant difference in the "self-absorbed" subscale.

3.4. Adaptive toileting skills

In Table 3, adaptive toileting skills in the total sample, as well as specific symptoms in individuals with NE, DUI and FI are outlined in the three age groups. The majority of individuals wore diapers all day (87%) and needed help with toileting.

Table 1
Descriptive data, somatic conditions and subgroups of incontinence of the total sample.

	Total (N = 47)
Mean age in years (SD)	13.0 (6.8)
Males% (n)	42.6 (20/47)
Females% (n)	57.4 (27/47)
Medical conditions% (n)	91.5 (43/47)
Seizures	85.1 (40/47)
Heart defects	42.6 (20/47)
Hirschprung disease	38.3 (18/47)
Urogenitary/renal tract anomalies	36.2 (17/47)
Clinical DBC[a] % (n)	39.1 (18/46)
DBC-P Total mean percentile (SD)	48.5 (22.9)
DBC-A Total mean percentile (SD)	54.4 (26.8)
Incontinence overall[b] % (n)	97.7 (42/43)
Nocturnal Enuresis (NE)	74.4 (32/43)
Daytime Urinary Incontinence (DUI)	76.2 (32/42)
Fecal Incontinence (FI)	81.4 (35/43)
Constipation% (n)	28.6 (12/42)
Combinations of Incontinence[c]	n
NE isolated	2
DUI isolated	1
NE + DUI	3
FI isolated	4
FI + DUI	3
FI + DUI + NE	24
No incontinence	1

DBC = Developmental Behavior Checklist; TBPS = Total Behavior Problem Score.
[a] Clinical DBC is defined as a TBPS > 46 in the DBC-P or a TBPS > 51 in the DBC-A.
[b] At least one subtype of incontinence.
[c] Data available from n = 38.

Table 2
Incontinence, constipation and clinical DBC over the age groups.

	Total N = 47	Children (4–12 years) N = 26	Teens (13–17 years) N = 13	Adults (≥18 years) N = 8	Significance[a]
Mean age in years (SD)	13.0 (6.8)	8.4 (2.9)	15.1 (1.5)	24.8 (5.1)	
Incontinence overall% (n)	97.7 (42/43)	95.8 (23/24)	100 (12/12)	100 (7/7)	n. s.
Nocturnal Enuresis% (n)	74.4 (32/43)	70.8 (17/24)	90.9 (10/11)	62.5 (5/8)	n. s.
Daytime Urinary Incontinence% (n)	76.2 (32/42)	72.7 (16/22)	91.7 (11/12)	62.5 (5/8)	n. s.
Fecal Incontinence% (n)	81.4 (35/43)	88.0 (22/25)	75.0 (9/12)	66.7 (4/6)	n. s.
Constipation% (n)	28.6 (12/42)	12.0 (3/25)	54.5 (6/11)	50.0 (3/6)	**.031***
Clinical DBC[b] % (n)	39.1 (18/46)	46.2 (12/26)	25.0 (3/12)	37.5 (3/8)	n. s.
DBC-P/A Total mean percentile (SD)		49.5 (23.6)	48.7 (20.4)	54.4 (26.8)	
DBC Mean item scores[c] (SD):					
Total		0.46 (0.2)	0.46 (0.2)	0.38 (0.2)	n. s.
Disruptive/Antisocial		0.36 (0.2)	0.35 (0.3)	0.43 (0.4)	n. s.
Self-Absorbed		0.70 (0.2)	0.69 (0.2)	0.32 (0.2)	**.001****
Communication Disturbance		0.33 (0.3)	0.45 (0.3)	0.55 (0.3)	n. s.
Anxiety		0.47 (0.4)	0.35 (0.3)	0.14 (0.2)	n. s.
Depression[d]		n. a.	n. a.	0.49 (0.3)	n. a.
Social Relating		0.30 (0.2)	0.33 (0.3)	0.26 (0.1)	n. s.

SD = standard deviation; DBC = Developmental Behavior Checklist; n. a. = not available.
[a] Fisher's Exact tests for categorial data; univariate analyses of variance (ANOVAs) for parametric data; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; n. s. = not significant ($p \geq 0.05$).
[b] Clinical DBC is defined as a TBPS > 46 in the DBC-P or a TBPS > 51 in the DBC-A.
[c] Mean Items scores are calculated as the scale raw score divided by the number of items in the scale.
[d] The subscale "depression" is only a subscale in the DBC-A.

The ability to use the toilet for micturition increased significantly with age (from 11.5% in children to 75% in adults). There was a trend that the ability to use the toilet for bowel movements increased over age, too (from 11.5 to 50%).

In individuals with NE, most wet the bed every night. This rate remained high over age. No individual had a dry period before. The ability to wake up after wetting or to go to the toilet at night increased significantly with age. In individuals

Table 3
Adaptive toileting skills and symptoms of incontinence over the age groups.

	Total	Children (4–12 years)	Teens (13–17 years)	Adults (≥18 years)	Significance[b]
Adaptive toileting skills[a] (Total N)	47	26	13	8	
Does he/she wear diapers during the day? %	87.0	88.5	91.7	75.0	n. s.
Does he/she use the toilet to pass urine? %	25.5	11.5	23.1	75.0	**.021***
Does he/she use the toilet to pass stools? %	21.7	11.5	25.0	50.0	n. s.
Does he/she tell you when he/she has to go to the toilet? %	17.4	16.0	15.4	25.0	n. s.
Does he/she need help when he/she goes to the toilet? %	82.8	79.2	76.9	100	n. s.
Nocturnal enuresis[a] (Total N)	42	17	10	5	
How often does he/she wet the bed?					
Every night	65.6	76.5 (13)	60.0 (6)	40.0 (2)	n. s.
2x/week or more	25.0	17.6 (3)	30.0 (3)	40.0 (2)	
1x/month or more	9.4	5.9 (1)	10.0 (1)	20.0 (1)	
Has he/she ever been dry during the night for more than 6 months? %	0	0	0	0	
Does he/she wake up to go to the toilet? %	9.7	0	0	60.0 (3)	**.002****
Is he/she a deep sleeper, i. e. difficult to wake up? %	21.9	23.5 (4)	20.0 (2)	20.0 (1)	n. s.
Does he/she wake up after wetting the bed? %	12.5	0	10.0 (1)	60.0 (3)	**.009****
Daytime urinary incontinence[a] (Total N)	32	16	11	5	
How often does he/she wet himself/herself during the day?					
Every day	84.4	93.8 (15)	81.8 (9)	60.0 (3)	n. s.
2x/week or more	12.5	6.3 (1)	9.1 (1)	40.0 (2)	
1x/month or more	3.1	0	9.1 (1)	0	
How many times a day does he/she wet?					
Once or twice	32.3	25.0 (4)	30.0 (3)	60.0 (3)	n. s.
3–4 times	45.2	43.8 (7)	50.0 (5)	40.0 (2)	
5–6 times	19.4	25.0 (4)	20.0 (2)	0	
More	3.2	6.3 (1)	0	0	
Does he/she notice when he/she wets?	37.9	35.7 (5)	36.4 (4)	50.0 (2)	n. s.
Fecal incontinence[a] (Total N)		22	9	4	
How many times a week does he/she soil?					
Every day	68.6	72.7 (16)	66.7 (6)	50.0 (2)	n. s.
2x/week or more	25.7	22.7 (5)	22.2 (2)	50.0 (2)	
1x/month or more	5.7	4.5 (1)	11.1 (1)	0	
How often does he/she soil per day?					
Once or twice	68.8	61.9 (13)	87.5 (7)	66.7 (2)	n. s.
3–4 times	28.1	33.3 (7)	12.5 (1)	22.2 (1)	
5–6 times	3.1	4.8 (1)	0	0	
How large are the stool masses?					
Smears	12.9	0	28.6 (2)	50.0 (2)	**.005****
Small amounts	3.2	0	14.3 (1)	0	
Moderate amounts	77.4	95.0 (19)	42.9 (3)	50.0 (2)	
Large amounts	6.5	5.0 (1)	14.3 (1)	0	
What is the consistency of his/her stool?					
hard	20.0	22.7 (5)	11.1 (1)	25.0 (1)	n. s.
soft	37.1	36.4 (8)	55.6 (5)	0	
watery	5.7	0	11.1 (1)	25.0 (1)	
Varying consistency	37.1	40.9 (9)	22.2 (2)	50.0 (2)	
Does he/she soil during sleep/the night?	51.4	40.9 (9)	66.7 (6)	75.0 (3)	n. s.

Numbers in parentheses refer to the absolute numbers.
[a] The percentage of the answer "yes", if not otherwise specified.
[b] Fisher's Exact tests; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; n. s. = not significant ($p \geq 0.05$).

with DUI, no difference between the age groups was found regarding the rates of wetting frequency or the ability to notice wetting.

The frequency of FI did not change over the age, but there was a significant change in the size of stool masses during soiling, as adults had a higher rate of "smears". In children, stool masses were more often "moderate" or "large", whereas in teens or adults more smears or small amounts of soiling occurred. The consistency and episodes of nighttime soiling did not vary between the groups.

4. Discussion

4.1. Incontinence overall

This is the first study that examines incontinence systematically in MWS. The results show that incontinence is a major problem in MWS, as nearly all individuals of the sample were affected. The rates were much higher than those of persons

with severe ID and more comparable to those with profound ID (85–100%) (von Wendt et al., 1990). The combinations of incontinence reveal that two thirds of persons with MWS have all three subtypes (NE, DUI, FI).

As there are no other systematic studies on MWS and incontinence, comparisons with other genetic syndromes could be revealing. Even though MWS has some similarity to Angelman Syndrome (ANG) (seizures, severe ID, sociability) (Evans et al., 2012; Mowat, Wilson, & Goossens, 2003), incontinence rates differ in both syndromes. Incontinence in ANG ranges between 89 and 95% for NE, 43–54% for DUI and 61% for FI showing that NE is the most common subtype (Didden, Korzilius, Smits, & Curfs, 2004; Laan, Den Boer, Hennekam, Renier, & Brouwer, 1996; Radstaake et al., 2013). In the present sample, overall incontinence in MWS (97.7%) was even higher than in ANG. But in contrast, FI is the most common subtype (81.4%) followed by DUI and NE (74–76%) in MWS, while persons with ANG were most affected by NE.

4.2. Fecal incontinence and HSCR

An explanation why FI is the most common incontinence subtype in MWS could be the strong association between MWS and HSCR. In a review of MWS cases, HSCR is estimated to be present in 45% of cases (Coyle & Puri, 2015), comparable to the rates in the present sample (38.3%). Complications after HSCR surgery are frequent in MWS (Bonnard et al., 2009), as 38.5% of MWS patients continued to have further symptoms as constipation or soiling despite surgery (Coyle & Puri, 2015).

Despite the high prevalence of HSCR, the rates of constipation in childhood were low, whereas half of adolescents and adults were affected. It could be speculated, that parents of affected children pay more attention to regular bowel movements after HSCR surgery (which is performed in childhood) and therefore reduce the risk of constipation (e.g. by treatment with laxatives etc.). In later age, it can be speculated further that bowel management is possibly less strict so that some individuals may develop behaviours (e.g. a low-fiber diet, insufficient liquid intake) predisposing towards constipation. Persons with ID are known to have insufficient liquid intake and higher rates of constipation (van Laecke, Raes, Vande Walle, & Hoebeke, 2009). Case reports show that constipation is not necessarily associated with HSCR: about the half of cases without HSCR (3 out of 6 and 6 out of 10 cases, respectively) had constipation, too (Adam et al., 2006; Garavelli et al., 2009). The possibility of very short segment HSCR ought to be considered in these individuals.

4.3. Associations with intellectual disability

The persisting high rates of incontinence over age could be due to the severity of ID. In other syndromes with moderate or mild ID (such as Noonan, Williams, Fragile-X- or Prader-Willi Syndrome), incontinence rates decreased from childhood into adulthood (Equit, Piro-Hussong, Niemczyk, Curfs, & von Gontard, 2013; Niemczyk, Equit, Borggrefe-Moussavian, Curfs, & Von Gontard, 2015; von Gontard et al., 2015). According to von Wendt et al. (1990), the level of intellectual impairment plays a major role in gaining bladder and bowel control, not only in ID in general, but also in specific syndromes.

In addition, severe ID is often associated with somatic disabilities or medical conditions, which could lead also to higher rates of somatic (not functional) forms of incontinence that cannot be diagnosed by a questionnaire. In the present study, 36.2% persons with MWS had anomalies of the genitourinary or renal tract. This high rate could therefore indicate higher rates of organic incontinence, but these can only be assessed by a medical examination in the individual patient.

4.4. Differences between age groups

Although incontinence rates do not decrease over age, there are indicators that some aspects of bladder and bowel control do improve in MWS. The majority (75–91.7%) of persons with MWS in the present study still wore diapers all day indicating that they were not toilet-trained, yet. However, other adaptive skills (ability to use the toilet for micturition and bowel movements) did improve with age, 75% and 50% of adults were able to use the toilet to pass urine or stools, respectively. These increasing skills show that persons with MWS can be toilet-trained, as had been shown in case reports (Adam et al., 2006). In persons with FI, the stool masses diminished from childhood to adulthood which also indicates that bowel control could have improved. In adults with NE, the rates of waking up at night to go to the toilet (nocturia) or after wetting are much higher than in adolescents or children with MWS. As NE is caused by maturational deficits in centers of the brainstem (Franco et al., 2015), the improvement of nighttime waking in MWS could be a sign of improving maturational processes.

4.5. Behavioral problems

In the present sample, behavioral symptoms were present in 39.1% of individuals with MWS which is similar to the rates of Evans et al. (33.3%) in a comparable group (Evans et al., 2012). These psychological symptoms were also related to sleep problems (Evans et al., 2016). In the present study no significant associations between psychological symptoms and incontinence were found, in contrast to other genetic syndromes with mild ID (Noonan, Williams, Fragile-X-Syndrome) (Equit et al., 2013; Niemczyk et al., 2015; von Gontard et al., 2015). The difference in level of ID is the most likely explanation, as the association between psychopathology and incontinence is found only in children with average intelligence (Franco et al., 2015) or mild ID, while incontinence in severe ID is possibly more closely associated with somatic conditions.

4.6. Strengths and limitations

A major strength of the study is the novelty of the results, i. e. that it is the first description of incontinence and associated factors in a larger group of individuals with MWS. Further, validated questionnaires were used and incontinence was diagnosed according to DSM-5 and ICCS criteria. Limitations are the cross-sectional design and that due to study design further clinical examinations (IQ test, physical examination, sonography and uroflowmetry) could not be performed.

5. Conclusions

The present study shows that nearly all individuals with MWS are affected by incontinence. Although some adaptive toileting skills improve from childhood to adulthood (e.g. using the toilet, waking at night to urinate, smaller soiled stool amounts), most individuals still wear diapers. It is presumed that the high rates of incontinence in MWS emerge from a co-existence of functional and organic incontinence forms.

5.1. Clinical implications

Nearly all individuals with MWS are affected by incontinence, which is often neglected because of other medical conditions. Due to higher rates of constipation in older individuals, these should always be screened for bowel movement frequency and consistency of stools, which are good indicators for constipation. Further, all individuals should be screened for psychological symptoms. As effective interventions for incontinence are available for persons with ID in general (von Gontard, 2013), assessment and treatment of incontinence are recommended in persons with MWS, as well.

References

American Psychiatric Association (APA). (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, D.C: APA (DSM 5).

Adam, M. P., Schelley, S., Gallagher, R., Brady, A. N., Barr, K., Blumberg, B., & Hudgins, L. (2006). Clinical features and management issues in Mowat-Wilson syndrome. *American Journal of Medical Genetics, Part A, 140*(24), 2730–2741. http://dx.doi.org/10.1002/ajmg.a.31530

Adam, M. P., Justice, A. N., Bean, L. J. H., & Fernhoff, P. M. (2008). Mowat-Wilson syndrome with craniosynostosis: A case report. *American Journal of Medical Genetics, Part A, 146*(2), 245–246. http://dx.doi.org/10.1002/ajmg.a.32075

Austin, P. F., Bauer, S. B., Bower, W., Chase, J., Franco, I., Hoebeke, P., & Nevéus, T. (2015). The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the international children's continence society. *Neurourology and Urodynamics*, http://dx.doi.org/10.1002/nau.22751

Bonnard, A., Zeidan, S., Degas, V., Viala, J., Baumann, C., Berrebi, D., & El Ghoneimi, A. (2009). Outcomes of hirschsprung's disease associated with Mowat-Wilson syndrome. *Journal of Pediatric Surgery*, *44*(3), 587–591. http://dx.doi.org/10.1016/j.jpedsurg.2008.10.066

Coyle, D., & Puri, P. (2015). Hirschsprung's disease in children with Mowat-Wilson syndrome. *Pediatric Surgery International*, *31*(8), 711–717. http://dx.doi.org/10.1007/s00383-015-3732-x

De Gennaro, M., Niero, M., Capitanucci, M. L., Von Gontard, A., Woodward, M., Tubaro, A., & Abrams, P. (2010). Validity of the international consultation on incontinence questionnaire-pediatric lower urinary tract symptoms: A screening questionnaire for children. *Journal of Urology*, *184*(4 Suppl), 1662–1667.

Didden, R., Korzilius, H., Smits, M. G., & Curfs, L. M. G. (2004). Sleep problems in individuals with angelman syndrome. *American Journal on Mental Retardation*, *109*(4), 275–284. http://dx.doi.org/10.1352/0895-8017(2004)109<275:SPIIWS>2.0. CO;2

Einfeld, S., & Tonge, B. (2002). *Manual for the developmental behaviour checklist – Primary carer version (DBC-P) & teacher version (DBC-T)* (2nd ed.). Clayton, Melbourne: Monash University Centre for Developmental Psychiatry and Psychology.

Equit, M., Piro-Hussong, A., Niemczyk, J., Curfs, L., & Von Gontard, A. (2013). Elimination disorders in persons with Prader-Willi and Fragile-X syndromes. *Neurourology and Urodynamics*, *32*(7), 986–992.

Evans, E., Einfeld, S., Mowat, D., Taffe, J., Tonge, B., & Wilson, M. (2012). The behavioral phenotype of Mowat-Wilson syndrome. *American Journal of Medical Genetics, Part A, 158 A*(2), 358–366. http://dx.doi.org/10.1002/ajmg.a.34405

Evans, E., Mowat, D., Wilson, M., & Einfeld, S. (2016). Sleep disturbance in Mowat-Wilson syndrome. *American Journal of Medical Genetics, Part A*, *170*(3), 654–660. http://dx.doi.org/10.1002/ajmg.a.37502

Franco, I., Austin, P. F., Bauer, S., Von Gontard, A., & Homsy, Y. (Eds.). (2015). *Pediatric incontinence – Evaluation and clinical management*. Chicester, UK: Wiley Blackwell.

Garavelli, L., Zollino, M., Cerruti Mainardi, P., Gurrieri, F., Rivieri, F., Soli, F., & Neri, G. (2009). Mowat-Wilson syndrome: Facial phenotype changing with age: Study of 19 italian patients and review of the literature. *American Journal of Medical Genetics, Part A*, *149*(3), 417–426. http://dx.doi.org/10.1002/ajmg.a.32693

Laan, L. A. E. M., Den Boer, A. T., Hennekam, R. C. M., Renier, W. O., & Brouwer, O. F. (1996). Angelman syndrome in adulthood. *American Journal of Medical Genetics*, *66*(3), 356–360. http://dx.doi.org/10.1002/(SICI)1096-8628(19961218)66:3<356:AID-AJMG21>3.0. CO;2-K

Mohr, C., Tonge, B., Einfeld, S., & Taffe, J. (2011). *Manual for the developmental behaviour checklist for adults (DBC-A)*. Clayton, Melbourne: Monash University Centre for Developmental Psychiatry and Psychology [revised].

Mowat, D., & Wilson, M. (2010). Mowat-Wilson syndrome. In *Management of genetic syndromes* (3rd ed., pp. 517–527). http://dx.doi.org/10.1002/9780470893159

Mowat, D. R., Croaker, G. D. H., Cass, D. T., Kerr, B. A., Chaitow, J., Adès, L. C., & Wilson, M. J. (1998). Hirschsprung disease, microcephaly, mental retardation, and characteristic facial features: Delineation of a new syndrome and identification of a locus at chromosome 2q22-q23. *Journal of Medical Genetics*, *35*(8), 617–623.

Mowat, D. R., Wilson, M. J., & Goossens, M. (2003). Mowat-Wilson syndrome. *Journal of Medical Genetics*, *40*(5), 305–310.

Niemczyk, J., Equit, M., Borggrefe-Moussavian, S., Curfs, L., & von Gontard, A. (2015). Incontinence in persons with Noonan syndrome. *Journal of Pediatric Urology*, *11*(4), 201.e1. http://dx.doi.org/10.1016/j.jpurol.2015.06.002

Radstaake, M., Didden, R., Giesbers, S., Korzilius, H., Peters-Scheffer, N., Lang, R., & Curfs, L. M. G. (2013). Incontinence in individuals with Angelman syndrome: A comparative study. *Research in Developmental Disabilities*, *34*(11), 4184–4193.

van Laecke, E., Raes, A., Vande Walle, J., & Hoebeke, P. (2009). Adequate fluid intake, urinary incontinence, and physical and/or intellectual disability. *Journal of Urology*, *182*(4 Suppl), 2079–2084.

von Gontard, A., Niemczyk, J., Borggrefe-Moussavian, S., Wagner, C., Curfs, L., & Equit, M. (2015). Incontinence in children, adolescents and adults with Williams syndrome. *Neurourology and Urodynamics*, http://dx.doi.org/10.1002/nau.22866

von Gontard, A. (2012a). Encopresis. In J. M. Rey (Ed.), *IACAPAP e-textbook of child and adolescent mental health*. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions (Accessed 11 March 2016). http://iacapap.org/wp-content/uploads/C.5-ENCOPRESIS-0072012.pdf
von Gontard, A. (2012b). Enuresis. In J. M. Rey (Ed.), *IACAPAP e-textbook of child and adolescent mental health*. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions (Accessed 11 March 2016). http://iacapap.org/wp-content/uploads/C.4-ENURESIS-072012.pdf
von Gontard, A. (2013). Urinary incontinence in children with special needs. *Nature Reviews Urology*, *10*(11), 667–674.
von Wendt, L., Simila, S., Niskanen, P., & Jarvelin, M. (1990). Development of bowel and bladder control in the mentally retarded. *Developmental Medicine and Child Neurology*, *32*(6), 515–518.