Received: 10 February 2020 | Accepted: 3 June 2020

DOI: 10.1002/nau.24436

ORIGINAL CLINICAL ARTICLE

Neurourology Urodynamics ICS SUFU WILEY

Incontinence in persons with tuberous sclerosis complex

Oriana Clasen[1] | **Justine Hussong**[1] | **Catharina Wagner**[1] | **Marina Flotats-Bastardas**[2] | **Sascha Meyer**[2] | **Michael Zemlin**[2] | **Alexander von Gontard**[1]

[1]Department of Child and Adolescent Psychiatry, Saarland University Medical Center, Homburg, Germany

[2]Department of Pediatric Neurology, Saarland Tuberous Sclerosis Complex Center, Saarland University Medical Center, Homburg, Germany

Correspondence
Oriana Clasen, Department of Child and Adolescent Psychiatry, Saarland University Medical Center, Homburg 66421, Germany.
Email: oriana.clasen@uks.eu

Abstract

Aims: Tuberous sclerosis complex (TSC) is a multisystem genetic disorder caused by a mutation in the TSC1 or TSC2 gene with a broad spectrum of physical and psychological manifestations. The aim of the study was to examine incontinence, psychological problems, and adaptive behavior skills in patients with TSC.

Methods: Through a worldwide TSC support group, 26 children (4-17 years) and 15 adults (18-50 years) with TSC were recruited (38.1% male, mean age 16.4 years). Parents or care-givers completed the Developmental Behavior Checklist (DBC), the Parental Questionnaire: Enuresis/urinary Incontinence, and the Vineland Adaptive Behavior Scales (3rd edition).

Results: A total of 60.0% of the participants had nocturnal enuresis (NE), 51.3% daytime urinary incontinence (DUI) and 52.4% fecal incontinence (FI). 65.4% of children and 50.0% of adults had a clinically relevant DBC score. Psychological symptoms were associated with at least one subtype of incontinence. The mean adaptive behavior composite (ABC) score of the patients was 57.2 (SD = 26.1), with 38.1% in the average or below-average range (IQ >70), 26.2% with a mild, 11.9% with a moderate and 23.8% with a severe/profound intellectual disability. The incontinence rate was significantly higher in the groups with a lower ABC score.

Conclusion: A substantial proportion of patients with TSC are affected by incontinence and psychological symptoms. Incontinence was higher in persons with lower adaptive skills and those with at least one type of incontinence showed a significantly higher DBC score. As incontinence and psychological problems affect daily functioning and well-being, assessment, and treatment are recommended.

KEYWORDS

daytime urinary incontinence, Developmental Behavior Checklist, encopresis, nocturnal enuresis, tuberous sclerosis complex, Vineland Adaptive Behavior Scales

Oriana Clasen and Justine Hussong contributed equally to this study.

1 | INTRODUCTION

Tuberous sclerosis complex (TSC) is a rare genetic disorder with an incidence of approximately 1:11.180-1:22.360 live births[1] that can affect multiple organ systems. It is an autosomal dominant disorder caused by a mutation or deletion in either the TSC1 (chromosome 9) or TSC 2 (chromosome 16) gene, leading to an overstimulation of the mTOR pathway.[2] Patients with a TSC2-gene mutation tend to be affected with a more severe phenotype.[3]

TSC is characterized by anomalies of the skin (eg, facial angiofibromas, fibrous cephalic plaques, ungual fibromas, hypomelanotic macules), kidney (angiomyolipomas, renal cell carcinomas, cysts), heart (arrhythmias, rhabdomyomas), brain (subependymal giant cell astrocytomas, subependymal nodules and cortical dysplasias, seizures, intellectual disability/developmental delay, psychiatric illness), and lungs (lymphangioleiomyomatosis, multifocal micronodular pneumonocyte hyperplasia). Tumors of the central nervous system are the leading cause of morbidity and mortality, followed by renal diseases.[2]

Besides neurological, skin, and renal manifestations TSC-associated neuropsychiatric disorders (TAND) can occur in patients. This term describes a range of neuropsychiatric manifestations including behavioral, psychiatric, intellectual, academic, and psychosocial problems.[4] TSC patients have an increased risk of a comorbid autism spectrum disorder, attention deficit hyperactivity disorder, disruptive behavior as well as high levels of anxiety and depressive disorders.[2] The estimated prevalence of intellectual disability in persons affected by TSC ranges from 50% to 65%.[5] The IQ-distribution is bimodal with one peak in the range of severe ID and a second peak with an almost normal IQ-distribution. Approximately a third of all children with TSC have academic difficulties.[5] Another measure for intellectual ability is the adaptive behavior composite (ABC) standard score. It has an IQ scale (mean = 100, SD = 15) and correlates significantly to the IQ of the individual. The ABC score includes scores of different adaptive behavior domains.

Functional incontinence includes daytime urinary incontinence (DUI), nocturnal enuresis (NE), and fecal incontinence (FI). NE and DUI are diagnosed according to the International Children's Continence Society (ICCS) from the age of 5 years onwards (with a wetting frequency of at least 1×/month) after exclusion of organic causes.[6] Encopresis is diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5) from the age of 4 years onwards (occurring at least 1×/month) after exclusion of organic causes. Non-retentive FI can be differentiated from functional constipation according to ROME-IV criteria.[7]

In typically developing children, the prevalence is approximately 5% to 10% for NE, 6% for DUI, and 1% to 8% for FI, with decreasing rates into adolescence and adulthood.[8] In individuals with intellectual disability (ID), incontinence is more prevalent (30%-39% in 7-year-olds, 19%-20% in 20-year-olds) and is associated with the degree of intellectual disability (ID).[9]

In children with TSC estimated 80% were affected by renal disease, for example, angiomyolipoma of the kidney or renal cystic disease.[2]

In the study by Backes et al of nonorganic (functional) incontinence, 2 of 16 boys with TSC had NE and only one FI. Associated symptoms were not assessed and severely affected children with TSC were excluded.[10]

Due to the lack of previous studies, the aim of this study was to analyze the prevalence of subtypes of nonorganic (functional) incontinence (NE, DUI, FI) in individuals with TSC. Associations between incontinence, psychological symptoms, and adaptive abilities were examined. It was hypothesized that individuals with TSC show symptoms of incontinence and that the rate of incontinence increases with the degree of impairment of adaptive functions, as well as with psychological symptoms.

2 | MATERIALS AND METHODS

The study was announced on the homepage of the Tuberous Sclerosis Alliance Support Group (US) with study information and a link to a questionnaire. Questionnaires were provided in English and could be requested online by interested families. The packages were sent by mail to the families. After parents or caregivers gave their informed consent, they were asked to complete the questionnaires and send them back anonymously. Altogether, 111 questionnaires were sent over a time of 14 months (February 2017 until March 2018). The package included an information letter for parents or caregivers concerning the study and three questionnaires on psychological symptoms, incontinence, and adaptive skills. The study was approved by the local ethics committee.

Psychological symptoms were assessed using the Developmental Behavior Checklist (DBC).[11,12] 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). Caregivers or parents filled out either the adult version (DBC-A) for adults or the version of the DBC for children or adolescents (DBC-P). The version for adults (DBC-A) has an additional scale

for "Depression". Clinically relevant scores are defined as a TBPS >46 in the DBC-P and as a TBPS >51 in the DBC-A, respectively and represent psychological symptoms of the individual which cause distress and impairment and correlate with potential psychiatric diagnoses.[11,12] In addition, both versions of the DBC total scores can be expressed in percentiles according to norms for children and adults with mild, moderate, and severe intellectual disability.[11,12] The DBCt has a significant concurrent validity with questionnaires and expert rating (DBC-P: r = 0.72-0.86; DBC-A: r = 0.52-0.63) and high reliability (DBC-P: r = 0.80-0.83; DBC-A: r = 0.69-0.72).[11,12]

The "Parental Questionnaire: Enuresis/Urinary Incontinence"[13] and the "Encopresis Questionnaire – Screening Version"[14] assesses incontinence and associated symptoms, as well as voiding and stool behavior. The "Parental Questionnaire: Enuresis/Urinary Incontinence" consists of 41 items and has been validated with satisfying psychometric properties.[15] As defined by the ICCS, NE and DUI were diagnosed in persons older than 5 years when wetting occurs at least once per month.[6] According to DMS-5, FI was diagnosed from the age of 4 years when soiling occurs at least once per month.[16]

Adaptive behavior was measured with the Vineland Adaptive Behavior Scales, Third Edition (Vineland-III). There are three different comprehensive administration forms. We used the Parent/Caregiver Form (domain-level) in our study. It is the third revision of the first standardized measure of adaptive behavior.[17] The Vineland-III assesses three core adaptive behavior domains: daily living skills, or the ability to take care of one´s daily needs, communication (receptive, expressive, and written communication), and socialization. For children, 9 years and younger, the gross and fine motor skills can be assessed within the motor skills domain. In addition, the maladaptive behavior domain was added.[17] The Vineland-III can be administered for individuals from birth through age 90 years. An overall adaptive behavior composite (ABC) standard score can be measured, as well as standard scores for each of the adaptive behavior domains.[17] The Vineland-III questionnaire measures the adaptive behavior of an individual in a valid and reliable way and reports outcomes as the ABC-score. The ABC score has an IQ scale (mean = 100, SD = 15) and correlates significantly to the IQ of the individual. The Vineland scales evaluate whether or not a person could meet diagnostic criteria for intellectual disability, which was demonstrated in validation studies.[17] For further analyses, the ABC scores were subdivided in analogy to IQ levels.

Statistical analyses were performed using IBM SPSS Statistics 23 (IBM, Armonk, NY). Descriptive statistics, nonparametric tests (Chi Square tests, Fisher's Exact tests) for categorical data, and analysis of variance for parametric data (post hoc tests) were performed. At a P-value < .05, results were considered significant.

3 | RESULTS

Out of 111 families, 46 returned the packages (41.4%). Three participants were excluded due to an age of less than 4 years. One additional data set had to be excluded since the questionnaires were not complete. Thus, in total, we included 42 full data sets for the final analysis (37.8%). Three incontinence questionnaires had missing data and were also excluded from data analysis regarding incontinence analysis.

3.1 | Descriptive data

Descriptive data are shown in Table 1. The sample was divided into three age groups (children: 4-12 years, n = 21; teens: 13-17 years, n = 5; adults ≥18 years, n = 16). The mean age of the sample was 16.4 years (range 4-50 years). The sample consisted of 16 male and 26 female participants. Medical conditions concerning kidneys, ureters, bladder, and urethra were reported in 66.7% of cases. 90.5% of patients had current seizures or a history of seizures. 50% (n = 8) of the participants had a DBC-A score and in 65.4% (n = 17) a DBC-P score in the clinical range. The mean adaptive behavior composite (ABC) standard score for the whole sample group (n = 42) was 57.2 (SD = 26.1; range 20-119).

3.2 | Subtypes of incontinence

A total of 82.1% (n = 32) of 39 persons with TSC were affected by at least one subtype of incontinence. Data for (NE) was available for 40 persons, 24 of them were affected (60%). The rates for (DUI) were 51.3% (n = 20 of 39) and 52.4% for FI. Constipation was reported in 14 (35.0%) of 40 individuals.

3.3 | Incontinence, behavior and adaptive abilities over age groups

Data in different age groups are presented in Table 2. Rates of incontinence subtypes were high in all age groups, ranging from 90.5% in children to 69.2% in adults. Rates of NE, DUI, and FI were lower in the adult group, but the difference did not reach statistical significance. Also, constipation rates were similar between the age groups.

TABLE 1 Descriptive data, somatic conditions, subgroups of incontinence, and ABC score of the total sample

	Total (N = 42)
Mean age in years (SD)	16.4 (10.8)
Children: 4-12 y % (n)	50.0 (21)
Teens: 13-17 y % (n)	11.9 (5)
Adults ≥18 y % (n)	38.1 (16)
Males % (n)	38.1 (16)
Females % (n)	61.9 (26)
Kidneys, ureters, bladder, and urethra affected% (n)	68.3 (28/41)
Seizures or history of seizures% (n)	92.7 (38/41)
Clinical DBC[a,b]-P % (n)	65.4 (17/26)
Clinical DBC[a,b]-A % (n)	50.0 (8/16)
Incontinence overall[c] % (n)	82.1 (32/39)
Nocturnal enuresis (NE)	60.0 (24/40)
Daytime urinary incontinence (DUI)	51.3 (20/39)
Fecal incontinence (FI)	52.4 (22)
Constipation % (n)	33.3 (14/40)
Mean adaptive behavior (ABC) composite score (SD)	57.2 (26.1)
Domain communication, mean (SD)	54.7 (26.7)
Daily living skills, mean (SD)	55.0 (30.8)
Socialization (SD)	60.7 (25.8)
Motor skills (SD; n)	73.3 (18.0; 12)

[a]DBC = Developmental Behavior Checklist; TBPS = total behavior problem score.
[b]Clinical DBC is defined as a TBPS >46 in DBC-P or TBPS >51 in the DBC-A.
[c]At least one subtype of incontinence.

In addition, the rate of clinically relevant behavioral problems (DBC) was high (58.5% of the entire group), affecting 70.0% of children and 50.0% of adults (Table 2). There was no significant difference between age groups.

3.4 | Incontinence and DBC scores

Incontinence rates in individuals with clinically relevant psychological symptoms vs those with subclinical symptoms (according to DBC scores) are presented in Table 3.

Individuals with clinically relevant DBC scores show significantly higher rates of incontinence overall, NE and DUI, but not FI, than individuals with a subclinical DBC score.

3.5 | Incontinence and adaptive behavior categories

Table 4 shows the rates of NE, DUI, and FI over the three groups of the ABC score of the entire sample. The sample was divided into three groups according to their ABC scores in analogy to levels of intelligence: group 1 (ABC > 70) included individuals with an average ABC score (>85) (n = 4) and those with a subaverage score (85-70) (n = 12); group 2 (ABC 50-70) consisted of individuals with mild impairment (50-69) (n = 11); and group 3 (ABC <50) included those with moderate (35-49) (n = 5) and severe (<35) (n = 10) impairment.

The rates of at least one subtype of incontinence increased from 66.7% in the group with an ABC score >70 to 90.9% in the group with an ABC score 50 to 70 to 92.3% in the group with an ABC score <50, respectively. There was a significant difference in-between the two groups (ABC >70; ABC <50) regarding the prevalence of DUI (ABC >70 25.0%; ABC <50 83.3%; $P = .009$) as well as the prevalence of NE (ABC >70 35.7%; ABC <50 80.0%; $P = .050$). The rate of FI differed significantly ($P = .020$) between those with an ABC >70 (25.0%) and those with an ABC 50 to 70 (72.7%).

4 | DISCUSSION

This is the first study that analyzed the associations between incontinence, behavior, and adaptive skills in individuals with TSC. Our data confirmed and extend the results by Backes et al[10] who described a much smaller sample. To our knowledge, this is the second study to examine incontinence.

In our sample 62.0% (n = 26) had an estimated level of adaptive skills lower than 70, that is, corresponding with ID. Those results are consistent with other studies showing a prevalence between 50% to 65% of intellectual disability in people with TSC.[5] With a decreasing ABC score, the rates of incontinence increased in our group of participants. Hence, our results confirm our assumption that the prevalence of functional incontinence increases with the growing impairment of adaptive functions.[9] Except for FI, which showed the highest prevalence in the group of an ABC score 50 to 70, the other two subtypes presented the largest rate in the group of individuals with an ABC score of less than 70. Individuals with an average ABC score were underrepresented, probably due to selection effects in the recruitment process through an international support group. Therefore, the typical bimodal distribution of intelligence represented by adaptive levels was not apparent in this sample.[5]

TABLE 2 Incontinence, DBC score, and adaptive behavior score over age groups

	Total N = 42	Children (4-12 y) N = 21	Teens (13-17 y) N = 5	Adult (>18 y) N = 16	Significance[c]
Mean age in years (SD)	16.4 (10.8)	8.5 (2.8)	15.4 (1.7)	27.0 (10.1)	
Incontinence overall[a], % (n)	82.1 (32/39)	90.5 (19)	80.0 (4)	69.2 (9/13)	n.s.
Nocturnal enuresis, % (n)	60.0 (24/40)	65.0 (13/20)	80.0 (4)	46.7 (7/15)	n.s.
Daytime urinary Incontinence, % (n)	51.3 (20/39)	52.4 (11)	60.0 (3)	46.2 (6/13)	n.s.
Fecal incontinence % (n)	52.4 (22)	57.1 (12)	80.0 (4)	37.5 (6)	n.s.
Clinical DBC total score % (n)	58.5 (24/41)	70.0 (14/20)	40.0 (2)	50.0 (8)	n.s.
Mean ABC[b] score (SD)	57.2 (26.1)	62.9 (17.8)	38.6 (27.5)	55.6 (32.7)	n.s.

Abbreviations: ABC, adaptive behavior composite; DBC, Developmental Behavior Checklist; na, not available; n.s., not significant; SD, standard deviation.
[a]At least one subtype of incontinence.
[b]Adaptive behavior composite standard score.
[c]Fisher's exact test for non-parametric data and ANOVAs for parametric data (Welch test in case of variance inhomogeneity).

TABLE 3 Distribution of incontinence subtypes between individuals with a clinical vs a subclinical Developmental Behavior Checklist (DBC) score

	Clinical DBC score[b] (n = 24)	Subclinical DBC score (n = 17)	Significance
Incontinence overall % (n)	95.5 (21/22)	62.5 (10/16)	.028*[a]
Nocturnal enuresis (NE) % (n)	77.3 (17/22)	41.2 (7)	.022*
Daytime urinary incontinence (DUI) % (n)	63.6 (14/22)	31.3 (5/16)	.049*
Fecal incontinence (FI) % (n)	58.3 (14)	41.2 (7)	n.s.

[a]Fisher's exact tests.
[b]defined as a Total score >46 in the DBC-P and >51 in the DBC-A.

TABLE 4 Rates of nocturnal enuresis, daytime urinary incontinence, and fecal incontinence over three groups of the ABC score: average and subaverage IQ, mild and moderate intellectual disability.

	Total N = 42	ABC > 70 *N = 16* 1	ABC 50-70 N = 11, 2	ABC < 50 N = 15 3	*P*
Incontinence overall[a] % (n)	82.1 (32/39)	66.7 (10/15)	90.9 (10)	92.3 (12/13)	n.s.
Nocturnal enuresis % (n)	60.0 (24/40)	35.7 (5/14)	63.6 (7)	80.0 (12)	.050* (3 > 1)
Daytime urinary incontinence % (n)	51.3 (20/39)	25.0 (4)	54.5 (6)	83.3 (10/12)	.009** (3 > 1)
Fecal incontinence % (n)	52.4 (22)	25.0 (4)	72.7 (8)	66.7 (10)	.020* (2 > 1)

[a]At least one subtype of incontinence.
*P <.05.
**P <.01.

The overall rate of incontinence in individuals with TSC was 82.1% in our study, which is a higher rate than in persons with severe intellectual disability[9] but lower compared to individuals with other syndromes such as Mowat-Wilson syndrome and Angelman syndrome.[18,19] The rates of all three types of incontinence were comparable. The prevalence was much higher than in the study Backes et al, which had excluded all severely affected participants with TSC.

Even though the rates decreased over age, 69.2% continued to show symptoms of at least one type of incontinence as an adult. This could be due to the fact that, persons with a low adaptive skill have not received adequate treatment for incontinence and that especially adults might have not been examined for symptoms of incontinence.[20] In addition, 68.3% of patients were affected by upper and lower urinary tract disorders, which is much higher than in other syndromes. For example, in

one large study on Williams syndrome, the rate was only 8.1%.[21]

Compared to our findings, the rates of seizures or a history of seizures of 80% to 90% in previous studies[22] did not differ from our sample (92.7%). Due to the lack of information, the associations between the type, frequency, severity, and onset of seizures and incontinence could not be analyzed. Also, the number, size, and location of intracerebral fibromas, subependymal nodes, subependymal giant cell astrocytomas were not reported. In other syndromes such as Angelman syndrome, seizures and incontinence are clearly associated.[19]

More than 50% of the participants with a clinically relevant DBC score had significantly higher rates of incontinence, NE, and DUI than those without clinically relevant psychological symptoms. The typical behavioral phenotype of TSC includes attention-deficit/hyperactivity disorder, autism spectrum disorders, anxiety, and depressive disorders, all of which are associated with incontinence in typically developing children.[23] Overall, more than 90% of children and adults with TSC are affected by one or more TSC-associated neuropsychiatric disorders (TAND).[4,24] Despite this high rate, only 20% of TSC patients receive a diagnosis and treatment of their neuropsychiatric disorder, which is associated with higher parental stress.[4,24,25]

4.1 | Clinical implications

As treatment of functional, nonorganic is effective in persons with special needs and lower adaptive skills,[20] thorough assessment and specific treatment options should be offered to affected individuals with TSC.

4.2 | Strengths and limitations

This is the first description of incontinence in a group of people with TSC with different levels of adaptive skills. Also, validated instruments were used and the diagnoses of incontinence were established according to DSM-5 and ICCS criteria.

Limitations are the small sample size in some of the groups and the cross-sectional design that prohibits the analysis of causal associations. In addition, the study was based on questionnaire data and not on clinical examination. Due to the participation rate of 41.4% the sample is possibly not representative and selection biases cannot be excluded. We cannot rule out that possibly families more affected by children with incontinence mainly responded. Therefore, a potential higher prevalence of incontinence in our study could be the result.

5 | CONCLUSION

The present study shows that a high number of individuals with TSC are affected by incontinence into and throughout adulthood. Although the rates decreased over age, the majority still showed symptoms of incontinence after the age of 18 years. Especially adults with a low adaptive skill score showed a high prevalence of incontinence and clinically relevant behavioral problems. Therefore, incontinence and all comorbid symptoms and disorders should be evaluated in all age groups. Clinicians should offer treatment of incontinence regardless of the cognitive development of their patients.

ACKNOWLEDGMENTS

We like to thank the Tuberous Sclerosis Alliance Support Group (US) for their cooperation and support.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Oriana Clasen http://orcid.org/0000-0003-4153-5688
Justine Hussong http://orcid.org/0000-0003-1794-3817
Alexander von Gontard http://orcid.org/0000-0002-3579-6200

REFERENCES

1. Ebrahimi-Fakhari D, Mann LL, Poryo M, et al. Correction to: incidence of tuberous sclerosis and age at first diagnosis: new data and emerging trends from a national, prospective surveillance study. *Orphanet J Rare Dis*. 2019;14(1):106.
2. Northrup H, Koenig MK, Pearson DA, Au KS. Tuberous sclerosis complex. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. *GeneReviews® [Internet]*. Seattle, WA: University of Washington; 1999.
3. Kothare SV, Singh K, Chalifoux JR, et al. Severity of manifestations in tuberous sclerosis complex in relation to genotype. *Epilepsia*. 2014;55(7):1025-1029.
4. de Vries PJ, Whittemore VH, Leclezio L, et al. Tuberous sclerosis associated neuropsychiatric disorders (TAND) and the TAND Checklist. *Pediatr Neurol*. 2015;52(1):25-35.
5. Joinson C, O'Callaghan FJ, Osborne JP, Martyn C, Harris T, Bolton PF. Learning disability and epilepsy in an epidemiological sample of individuals with tuberous sclerosis complex. *Psychol Med*. 2003;33(2):335-344.
6. Austin PF, Bauer SB, Bower W, et al. 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. *Neurourol Urodyn*. 2016;35(4):471-481.
7. Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology*. 2006;130(5):1527-1537.
8. Franco I, Austin PF, Bauer S, von Gontard A, Homsy Y. *Pediatric Incontinence: Evaluation and Clinical Management*. Chicester, UK: Wiley Blackwell; 2015.

9. von Wendt L, Simila S, Niskanen P, Jarvelin MR. Development of bowel and bladder control in the mentally retarded. *Dev Med Child Neurol*. 1990;32(6):515-518.
10. Backes M, Genc B, Schreck J, Doerfler W, Lehmkuhl G, von Gontard A. Cognitive and behavioral profile of fragile X boys: correlations to molecular data. *Am J Med Genet*. 2000;95(2):150-156.
11. Einfeld S, Tonge B. *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; 2002.
12. Mohr C, Tonge B, Einfeld S, Taffe J. *Manual for the Developmental Behaviour Checklist for Adults (DBC-A)*. Clayton, Melbourne: Monash University Centre for Developmental Psychiatry and Psychology; 2011.
13. von Gontard AEnuresis. *IACAPAP e-Textbook of Child and Adolescent Mental Health*. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions; 2012. https://iacapap.org/content/uploads/C.4-ENURESIS-072012.pdf
14. von Gontard AEncopresis. *IACAPAP e-Textbook of Child and Adolescent Mental Health*. Geneva: International Association of Child and Adolescent Psychiatry and Allied Professions; 2012. https://iacapap.org/content/uploads/C.5-ENCOPRESIS-0072012.pdf
15. Niemczyk J, Schäfer S, Becker N, Wagner C, von Gontard A Evaluation of the 'parental questionnaire: enuresis/urinary incontinence'. In: Proceedings of the ICCS 2016 Annual Meeting 30 June-2 July 2016. Kyoto, Japan: International Children's Continence Society (ICCS) [Program and Abstracts; 2016 Abstract O 5-12]. 2016.
16. APA. *Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5)*. Washington, D.C.: APA; 2013.
17. Hill TL, Saulnier CA, Cicchetti D, Gray SAO, Carter AS. Vineland III. In: Volkmar FR, ed. *Encyclopedia of Autism Spectrum Disorders*. New York, NY: Springer; 2017:1-4.
18. Niemczyk J, Einfeld S, Mowat D, et al. Incontinence and psychological symptoms in individuals with Mowat-Wilson Syndrome. *Res Dev Disabil*. 2017;62:230-237.
19. Wagner C, Niemczyk J, Equit M, Curfs L, von Gontard A. Incontinence in persons with Angelman syndrome. *Eur J Pediatr*. 2017;176(2):225-232.
20. von Gontard A. Urinary incontinence in children with special needs. *Nat Rev Urol*. 2013;10(11):667-674.
21. von Gontard A, Niemczyk J, Borggrefe-Moussavian S, Wagner C, Curfs L, Equit M. Incontinence in children, adolescents and adults with Williams syndrome. *Neurourol Urodyn*. 2016;35(8):1000-1005.
22. Vignoli A, La Briola F, Turner K, et al. Epilepsy in TSC: certain etiology does not mean certain prognosis. *Epilepsia*. 2013;54(12):2134-2142.
23. von Gontard A, Baeyens D, Van Hoecke E, Warzak WJ, Bachmann C. Psychological and psychiatric issues in urinary and fecal incontinence. *J Urol*. 2011;185(4):1432-1436.
24. Krueger DA. Management of CNS-related disease manifestations in patients with tuberous sclerosis complex. *Curr Treat Options Neurol*. 2013;15(5):618-633.
25. Ebrahimi-Fakhari D, Hussong J, Flotats-Bastardas M, et al. Tuberous sclerosis complex associated neuropsychiatric disorders and parental stress: findings from a national, prospective TSC surveillance study. *Neuropediatrics*. 2019;50(5):294-299.

How to cite this article: Clasen O, Hussong J, Wagner C, et al. Incontinence in persons with tuberous sclerosis complex. *Neurourology and Urodynamics*. 2020;39:1842–1848. https://doi.org/10.1002/nau.24436