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DOES THE BLADDER HAVE A MEMORY? IS CHILDHOOD DYSFUNCTIONAL VOIDING RELATED TO BLADDER AND PELVIC FLOOR DYSFUNCTION IN ADULT WOMEN?

Hypothesis / aims of study
To assess the relationship between Childhood Dysfunctional Voiding (CDV) and Urinary Incontinence (UI) in adult women using an identical twin-sister study design that can potentially give insight into the influence of genetic variance. We hypothesised that a history of CDV would be positively related to urinary incontinence in adult women. We sought to assess the strength of this correlation with stress, urge and mixed UI. A second aim was to search for a possible impact of CDV on pelvic floor disorders and depressive episodes in adulthood, as these entities have been associated with UI in adult women.

Study design, materials and methods
An epidemiologic survey of 346 twins, of which 306 (89%) were identical was performed at two consecutive Twins-Day annual festivals in 2005 and 2006. All sister-twin pairs completed several validated questionnaires which included the Modified Dysfunctional Voiding Scoring System (DVSS), the Beck Depression Inventory-II (BDI-II), the PFDI-20 and the Pelvic Pain and Urgency/Frequency symptom scale (PUF). The DVSS contains a set of 10 questions related to a history of dysfunctional voiding in childhood. Each question has 5 possible answers; almost never=0, less than half the time = 1, half the time = 2, almost every time = 3, and not available. A total score is obtained by adding the scores of the 10 individual questions to obtain a total score ranging from 0-30. Dysfunctional voiding in girls has been shown to correlate with a score ≥ 6.[1] Mixed effects linear models for clustered data were used for group comparisons on summary scores and implemented in SAS PROC MIXED by including a random effect for twin pair to assess the total and individual DVSS scores in women with or without UI. Similarly, generalized estimating equations were used for comparisons on categorical measures and implemented in SAS PROC GENMOD with logit link function, binomial distribution and repeated measure effect for twin pair. A subgroup analysis was performed to asses the DVSS scores among women with stress, urge and mixed UI. Finally, DVSS scores were correlated to total and individual BDI-II scores (> 13 indicative of moderate-to-severe depression), PFDI-20 and PUF. Spearman Correlation Coefficients were calculated for each DVSS and PUF, PFDI-20 and BDI-II item. McNemar's tests and paired t-tests were used for the comparisons of identical discordant twin pairs. $P < 0.05$ was the criterion for statistical significance. SAS version 9.1 was used for all analyses.

Results: Available data for analysis was present for 344 twin-sisters, of which 89% were identical. There were 153 identical twin pairs of which 66% were concordant for CVD (in 27 pairs both twins were positive for CDV, while in 74 both twins did not report evidence of CVD). Of all participating twins with complete DVSS data, 114 (33%) scored ≥6 indicating a positive history of CDV vs. 230 (66.86%) scoring <6. Demographic characteristics were similar in women with and without a history of dysfunctional voiding in girls. Of participating twins, 93% were Caucasian, 14% Black, 4% Hispanic, 2% Asian, and 2% were of another race. BMI less than 25 was found in 53%, BMI 25-30 in 24% and >30 in 23%, 69% were premenopausal, 9% were current smokers, 18% were unemployed, over 9) had at least attended high school, 55% reported a yearly income of ≤$50K and 45% had at least 1 vaginal delivery.

Table 1: CDV in women with and without stress, Urge and Mixed UI.

	N (%) w/ total score ≥6	Mean total score ±SD	P value (versus women w/o UI)	Odds ratio (95% CI)
Women w/o UI (n=170)	48 (28%)	4.0 ± 3.6	-------	Reference:
Women w/ UI (n=166)	64 (39%)	4.8 ± 4.0	0.049	1.6 (1.05-2.5)
SUI (n=70)	22 (31%)	4.0 ± 3.8	0.377	1.2 (0.6-2.1)
Mixed UI (n=83)	36 (43%)	5.4 ± 4.1	0.002	1.9 (1.1-3.3)
Urge UI (n=13)	6 (46%)	5.7 ± 3.6	0.348	2.2 (0.7-6.8)

Table2: Correlation of BDI-II, PUF, PISQ-12 and PFDI scores in women with or without CDV.

	w/ CDV total score ≥6 Mean ± SD	without CDV, score <6, Mean ± SD	P value	Effect size (difference / SD)
BDI-II	9.2 ± 7.5	5.7 ±6.6	0.006	0.49
PUF	5.5 ± 4.7	3.4 ±3.6	<0.001	0.51
PISQ-12	35.3 ± 6.1	37.9 ±5.1	<0.001	0.46
PFDI – Total scores	37.3 ± 43.8	20.2 ±26.6	<0.001	0.50
PFDI-CRADI, mean ±SD	47.4 ±64.5	24.1 ±31.9	<0.001	0.50
PFDI-POPDI, mean ±SD	7.1 ±12.9	4.1 ±8.1	0.009	0.30
PFDI-UDI, mean ±SD	16.4 ±19.1	9.6 ±14.1	<0.001	0.42

Table 2a: Correlation of women with mild-or-no Depression with CDV

BDI-II total Depression scores	No CDV Score <6 (n=230) (%)	Positive CDV: score ≥6 (n=114) (%)	P value adjusted for twinning
0-13: Minimal	205 (89.13)	90 (78.95)	0.0447
14-19: Mild	10 (4.35)	12 (10.53)	

20-28: Moderate	13 (5.65)	9 (7.89)	
29-63: Severe	2 (0.87)	3 (2.63)	

Table 3: Correlation of CDV scores with worsening BDI-II, PUF, PISQ-12 and PFDI-20 scores

Spearman Correlation Coefficients (n = Observations)		p-value (adjusted for twinning)
PUF Total	0.25719 (n= 344)	<0.0001
BDI-II Depression Score	0.30094 (n= 344)	0.0002
PISQ Total	0.19418 (n= 278)	0.0033
PFDI-CRADI	0.25142 (n= 344)	<0.0001
PFDI-POPDI	0.20421 (n= 343)	
PFDI-UDI	0.21814 (n= 344)	

Interpretation of results

There were more women with a history of CVD in the group with adult UI vs. those without UI, p=0.049, Odds ratio 1.6 (95% CI 1.05 -2.50). This correlation persisted when looking at the discordant twins for CDV implying a possible impact which is beyond that of genetic variance (p-value paired analysis, = 0.0045). The most significant association was found in women with mixed UI (table 1). Women with a history of CDV had significantly worse total scores on the BDI-II (p=0.006), PUF (p<0.001), PISQ-12 (p<0.001) and PFDI (p<0.0001) questionnaires indicating significantly worse depressive episodes, painful bladder symptoms, pelvic floor disorders and worse sexual function (table 2 and 2a). Similarly, a significant linear correlation was found between a history of CDV (scores of ≥ 6 on the DVSS) and worsening scores on all these scales (table 3), indicating that higher CDV scores correlated with worse scores on these measuring instruments.

Concluding message

This study showed a significant association between CDV and UI in adult life. Amongst the sub-types of UI, the strongest correlation was noted in women with both stress and urge incontinence. The results indicate that a positive history of CVD is risk factor for later development of UI. As such it should be diagnosed and treated appropriately in childhood to decrease the potential risk of later UI and pelvic floor and sexual dysfunction in adult life. This underscores the importance of considering these entities as being closely related. A positive history of CDV in women that are first seen as adults for evaluation of pelvic floor disorders should include a thorough screening of these related entities to assess their risk and severity and provide timely diagnosis and treatment.

References

1. J Urol 2000;164:1011-5.

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CLINICAL TRIAL REGISTRATION: This clinical trial has not yet been registered in a public clinical trials registry.

HUMAN SUBJECTS: This study was approved by the Evanston Northwestern Healthcare Ethics Review Board and followed the Declaration of Helsinki Informed consent was obtained from the patients.