Psychological co-morbidities and functional neurological disorders in idiopathic urinary retention: International Consultation on Incontinence Research Society (ICI-RS) 2019

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Abstract

Aims:

Chronic urinary retention occurring in young women is poorly understood and a cause may not be found in a majority of cases. Different psychological co-morbidities and functional neurological symptom disorders (FNDs) have been reported, however these have been poorly explored.

Methods: At the International Consultation on Incontinence Research Society (ICI-RS) meeting in 2019, a panel of clinicians generated a proposal to explore the relationship between psychological co-morbidities, FNDs and urinary retention in women with chronic idiopathic urinary retention.

Results: Psychological co-morbidities such as depression and anxiety, and FNDs such as leg weakness and loss of consciousness, have been reported in women with idiopathic urinary retention. Individuals react differently to physical and emotional stressors, and experimental models have demonstrated a relationship between the stress response and developing urinary retention. Trauma, particularly sexual trauma, may be a shared risk factor for developing psychological co-morbidities and urinary retention. Children with voiding postponement often suffer from psychological co-morbidities and behavioral disturbances, however there is

no evidence to suggest that this progresses to urinary retention in adulthood. "Psychogenic urinary retention" has been described in the urology and psychiatry literature in the past, and anecdotal cases of successful voiding following psychotherapy have been reported, though the true pathophysiology of this entity is uncertain.

Conclusion: Psychological and functional disorder co-morbidities are reported in women with chronic urinary retention. The nature of the association between urinary retention and functional neurological disorder co-morbidities needs to be further explored in terms of a disorder of bladder-brain interaction.

Introduction

Chronic urinary retention occurring in young women is poorly understood. The urological assessment is useful in clinical phenotyping, to establish whether urinary retention is due to detrusor underactivity and/or bladder outlet obstruction (BOO) (1). There are several causes for chronic urinary retention, however an aetiology may not be found despite an extensive urological and neurological assessment (2) (3). In women with chronic idiopathic urinary retention, outcomes following treatment with sacral neuromodulation are mixed, however women with evidence of a functional BOO, specially with evidence for a primary disorder of external urethral sphincter relaxation by urethral pressure profilometry and/or urethral sphincter EMG (sometimes referred to as Fowler's syndrome), have shown a more favourable response to treatment (4) (5).

A number of studies have suggested the co-occurrence of different psychological and functional disorders in women with chronic idiopathic urinary retention (6) (7) (4) (8) (9) (10). From the available evidence, the commonest are affective disorders such as depression and anxiety, and functional disorders such as fibromyalgia, irritable bowel syndrome and functional neurological symptom disorders (FNDs) such as limb weakness

and non-epileptic attacks (9) (10). Historically, urological and psychological management have not been joined-up, and therefore the co-existence of urinary retention and psychological/ functional disorder co-morbidities has been poorly acknowledged and researched. The aim of this paper is to highlight gaps in the understanding of these co-morbidities, and to explore the nature of their relationship with urinary retention.

Methods

At the International Consultation on Incontinence Research Society (ICI-RS) held in Bristol, United Kingdom in 2019, a panel of clinicians participated in a discussion on psychological co-morbidities and FNDs reported in women with chronic idiopathic urinary retention. The panellists reviewed the different co-morbidities reported in the literature, how these were assessed, risk factors for developing these co-morbidities and outcomes following treatments. The panel also explored possible causal associations between these co-morbidities and developing urinary retention. From the discussions at the meeting and subsequent e-mail iterations, the panel proposed priority areas for further research.

Psychological co-morbidities

The two main classification systems of mental and behavioural disorders are the International Classification of Diseases ICD-11 (11) published by the World Health Organisation which has a chapter on mental and behavioural disorders, and the Diagnostic and Statistical Manual (DSM-5) (12) published by the American Psychiatric Association. Whilst the DSM is the most widely-used diagnostic system in the United States, the ICD is used more widely in Europe and other regions of the world. Mental, psychological and behavioural disorders reported in women with idiopathic urinary retention are collectively known as "psychological co-morbidities" in this paper.

In recent years, a number of screening questionnaires have become available to screen for different psychological co-morbidities. Many of these are self-reported and therefore can be completed by the patient. When assessing psychological co-morbidities in the medical setting, it is common to screen mainly for affective disorders (mood disorders), particularly depression and anxiety. Screening tools will usually have cut-off scores, suggesting a threshold score for 'caseness' and also an indication of severity of anxiety or depression. However, other psychological co-morbidities should be screened as well. In the United Kingdom, the Improving Access to Psychological Therapies (IAPT) programme has

transformed treatment of psychological disorders and provides evidence based treatments for people with anxiety and depression, implementing National Institute of Clinical Excellence (NICE) guidelines. The brief screening tools approved by IAPT for case identification are listed in Table 1 (13) (14) (15) (16) (17) (18) (19) (20) (21) (22) (23) (24). A broadband questionnaire recommended for children is the Child Behavior Checklist (25). A formal assessment of mental health difficulties includes a semi-structured clinical interview carried out by a qualified mental health professional, accompanied by mental health and physical examination and psychological testing. Structured interview schedules have been developed with the goal of improving diagnostic reliability.

Functional neurological symptom disorders

FNDs are characterised by the presence of altered voluntary motor or sensory function which are incompatible with recognized neurological or medical conditions. These include limb weakness, sensory disturbances, nonepileptic attacks and memory impairment, which cannot be explained by a neurological or other medical condition, and can cause a significant degree of distress warranting medical evaluation. FNDs can overlap with

other functional disorders such as fibromyalgia, chronic fatigue syndrome and irritable bowel syndrome. The term "conversion disorder" is retained under DSM-5, however psychological stressors may not be readily identifiable in all cases (26). Individuals with FNDs do not falsify physical or psychological signs, and therefore this condition is different from factitious disorders or malingering. Functional neurological symptom disorders have a reported incidence of 4 to 12 per 100000 population per year and a prevalence of 50 per 100000 population based on a community registry (27) (28) (29), and more prevalent in females(27).

A diagnosis of FND is made based upon the history and physical examination identifying specific neurological signs (26). A screening questionnaire for FNDs has been designed, however has limited sensitivity and specificity except for diagnosing "blackouts" (30).

Prevalence of co-morbidities in women with urinary retention

A number of functional and affective symptoms are known to co-exist with LUT disorders such as OAB and Bladder Pain Syndrome (31) (32) (33), as well as other visceral disorders such as irritable bowel syndrome (34). The burden of psychological co-morbidities and functional disorders amongst

women with idiopathic urinary retention is difficult to estimate, however from the evidence available prevalence of affective symptoms appears to be greater amongst OAB patients compared to urinary retention (9). The few studies that have evaluated psychological co-morbidities in women with idiopathic urinary retention have focused only on affective disorders, and the use of different screening questionnaires precludes comparison between studies (Table 2). These studies suggest the occurrence of different co-morbidities, namely depression requiring hospitalisation, "hysteria", depression, risk of somatisation, definitive somatoform disorder and unspecified psychiatric disorders (6) (7) (4) (8). The prevalence of other behavioural disorders such as phobias and PTSD, which are likely to have a relationship with lower urinary tract (LUT) functions, is unknown.

FNDs are under-recognised, partly due to the absence of a sufficiently robust screening tool, however from the evidence available the prevalence appears to be greater than in the general population (Table 2) (30) (10). In a cohort of 62 women with Fowler's syndrome, 24% had medically unexplained/"functional" symptoms which included loss of consciousness, limb weakness, sensory disturbance and memory impairment. Furthermore, almost a third (31%) had psychological co-morbidities such

as anxiety/depression or obsessive compulsive symptoms (10). Nearly 50% of women suffered from unexplained chronic abdomino-pelvic, back, leg or widespread pain (10) and use of opiate medications, which may interfere with LUT functions and cause urinary retention, was found to be common (2).

Vulnerability to developing psychological co-morbidities

In pelvic disorders with a substantial functional component, such as bladder pain syndrome, chronic pelvic pain syndrome and overactive bladder (OAB), it is hypothesised that an imbalance between resilience and vulnerability could lead to a sensitized defence reaction and alarm falsification in reaction to multiple cumulative threats. These threats could either be physical, such as an infection, or emotional, such as childhood adversity or emotional or sexual abuse (35). The balance between vulnerability and resilience is explained by a 3-hit concept of genetic predisposition, early-life environment and later-life environment (36). Therefore, stress in early life can influence brain plasticity with lasting effects, and epigenetic factors in combination with genetic predisposition can influence vulnerability or resilience to stress (37). For example, personality traits might predispose to vulnerability to functional urological

symptoms. "Neuroticism", a personality trait associated with a bias towards negative emotions, is associated with OAB (38). The importance of vulnerability was underscored by a large population-based study where urinary incontinence was significantly associated with psychological problems with feelings of vulnerability (39). To conclude, there is a difference to how people react to different kinds of physical and emotional stressors.

Relationship between stress and urinary retention-biological models

Chronic stress response can lead to changes in visceral organs. Studies in
mice have shown that mild social stress led to OAB behaviour(40) while
prolonged exposure to stress resulted in an increase in intermicturition
interval and voided volume, which are indicative of bladder underactivity.

These functional changes were accompanied by increased collagen
deposition and bladder wall remodeling (41). Bladder dysfunction therfore
progresses from overactivity to underactivity as the intensity and duration of
social stress increases, at least in experimental animal models (42).

Functional changes of voiding dysfunction may persist even after removal
of the stressor (43).

In male rats exposed to social stress, corticotropin releasing factor (CRF) receptor expression was upregulated in the Barrington's nucleus (44). In the hypothalamic–pituitary–adrenal (HPA) axis, CRF, a neuropeptide secreted by the paraventricular nucleus of the hypothalamus, is involved in the stress response by stimulating the pituitary release of ACTH which has inhibitory effects on the micturition pathway (45). In humans, urinary retention has been reported to occur following social stressors such as the loss of a loved one or a recent divorce (46), and social stress-induced voiding dysfunction seen in animal models could provide a biological explantion for this observation.

Sexual Trauma- shared risk factor for developing psychological comorbidities and chronic urinary retention?

Victims of rape or sexual abuse are prone to develop post-traumatic stress disorder (PTSD) and other psychological disorders as anxiety, depression and psychosis (47) (48) (49). The symptoms can occur immediately or with delayed onset. Additionally, occurrence of these disorders is more likely to be associated with a reduction in quality of life, increase in morbid obesity, marital instability, high use of medical care and somatic symptoms such as gastrointestinal symptoms and recurrent headache (50).

Moreover, patients who were sexually abused in childhood may also present with genitourinary symptoms. Zhao et al. recently reported an association between bullying and childhood LUT symptoms. This is also true for adults who have experienced sexual abuse, where storage symptoms such as nocturia, urinary frequency and urgency have been reported (51). However the prevalence of voiding difficulties amongst victims of sexual abuse has been poorly explored and Williams et al. (52) has reported a case of episodic urinary retention in a woman who experienced recurrent sexual trauma. Other pelvic symptoms reported by individuals who have experienced abuse include pelvic pain (53), dyspareunia and symptoms of prolapse (54) (55).

Voiding postponement in childhood –a precursor to developing urinary retention in adults?

Voiding postponement (VP) is defined as a habitual postponement of micturition by using holding maneuvers (56). Typical symptoms are low micturition frequency, feeling of urgency and possibly incontinence from a full bladder. Concomitantly, children with VP often suffer from psychological co-morbidities or behavioral disturbances such as Oppositional Defiant

Disorder (ODD). The prevalence of ODD is 2-5% and typical symptoms are a persistent angry and irritable mood, argumentative, defiant behavior and vindictiveness.

Voiding postponement can develop as a learned behavior, leading to shortterm positive effects of not needing to void in a specific social situation, however can persist despite negative consequences such as incontinence. This habit is often maintained for convenience, because of the fear of missing out (e.g. in play), due to unhygienic toilets in school, as a Some children develop VP without precursors, component of ODD. however the sequence from OAB, to VP, due to increased activation of pelvic floor muscles, to dysfunctional voiding and finally to underactive Typical signs of VP are abnormal uroflow curves bladder is possible. (plateau, staccato, intermittent), non-relaxed pelvic floor EMG activity, increased postvoid residual urine, increased maximal voided volumes, constipation, UTI's, dysfunctional family dynamics, lower quality of life and externalization of behavioural disorders. The mainstay of treatment of VP is timed voiding (7 times/day) with a continuous documentation using charts and positive reinforcement. Timer watches (or mobile phones) can

be useful adjuncts to serve as reminders to void regularly. In refractory cases, outpatient training programs have been shown to be efficient.

Voiding postponement affects 13.7% of adolescents (57) and occurs more likely if bladder control had been delayed or if daytime urinary incontinence, has been present in childhood. No studies have assessed the natural history of VP in boys and girls through adolescence to adulthood.

Discussion

"Psychogenic urinary retention"- terminology from a bygone era?

The Urology literature

Neuro-urology textbooks of more than 3 decades ago defined the umbrella term "psychogenic urinary dysfunction" (PUD) to cover not only urinary retention, but also any difficulty in voiding, paruresis and even overactive bladder (OAB) based on a diagnosis of exclusion of all urologic, gynecologic, and neurologic causes (58) (59). Manifest psychological features accompanying the LUT dysfunction were required to meet the definition of PUD (59) and PUD was considered to be a psychosomatic disorder affecting the lower urinary tract function (59). Nowadays, using the term PUD is unhelpful as it represents a heterogeneous group of patients with functional bladder disorders covering the spectrum from OAB

to bladder emptying problems. Moreover, investigations have become better refined to recognize a biological basis for disease. For example, urethral sphincter electromyography may demonstrate a characteristic abnormal pattern of activity in some women with urinary retention, and functional MRI studies suggest that brain responses to bladder filling are abnormal, which correlated with maximum urethral closure pressure (60).

However, few studies have evaluated the changes in psychological comorbidities following urological interventions for urinary retention. Only
affective symptoms have been studied and in a cohort of patients
undergoing SNM, significant improvements in voiding symptoms and
quality of life for idiopathic urinary retention were not accompanied with
improvements in depression/anxiety symptoms, in contrast to patient with
OAB where improvements were seen in patients with successful outcomes
(9). In an Italian registry study, most of the treatment failures belonged to
a group with psychological disorders such as "hysteria", depression and
hypochondria, suggesting a worse outcome in this group (7).

The Psychiatry literature

In the past, a psychological cause for urinary retention was considered acceptable, and Table 3 traces this history through earlier versions of the DSM (61) (62). This older literature documented a variety of predisposing and precipitating factors including major stressful life-events (63). A full review of the history of how psychological factors were understood to play a role in the aetiology of urinary retention is complicated by changes in diagnostic criteria and labelling, e.g. 'psychogenic urinary retention', 'hysteria', 'somatisation', conversion disorder, medically unexplained symptoms.

Reports of "successful treatment" of urinary retention by psychotherapy can in fact be found in the historical literature on 'Psychogenic urinary retention' (Table 4) (52) (64) (65) (66) (67, 68) (69) (70) (71) (72). In most cases, a history of conflict or trauma was reported and authors claimed that psychotherapy was found to be effective in relieving urinary retention, as well as improving other areas e.g. family and/or marital relationships.

Modern day classifications in urology and psychiatry practice however fail to mention "psychogenic urinary retention" and the reasons for this are unclear. The true pathophysiology of this entity is uncertain, however the availability of advanced urological and neurological diagnostic tests in the modern day (1) have helped to uncover a biological cause for urinary retention in a substantial number of patients who, in the past, would have been labelled to have "idiopathic urinary retention" (1).

Could the co-occurrence of FNDs and idiopathic urinary retention suggest a disorder of "bladder-brain interaction"?

Despite advances in diagnostic testing, the cause for urinary retention is found in only 40% of women (2). The search for putative organic mechanisms continues, however the high prevalence of functional disorders in women with idiopathic urinary retention compared to the general population is unlikely to be co-incidental. It is tempting to speculate that in some patients urinary retention may reflect a disorder of "bladderbrain interaction". For example, patients with functional motor weakness experience an unintentional loss of somatic function manifesting as limb Could some cases of chronic idiopathic urinary retention weakness. represent a functional disorder characterized by a loss of visceral organ (LUT) functions and a central failure to initiate detrusor contractions (73)? It is noteworthy that amongst patients with functional movement disorders, particularly functional dystonias, urinary retention is the commonest LUT

dysfunction reported (74). LUT functions are controlled centrally by an elaborate neuronal network distributed across different cortical regions, and bladder storage and emptying are learned behaviours (75).The ventromedial prefrontal cortex (PFC) is a key limbic structure that plays an important role in LUT control (76), as is involved in decision making in an emotional and social context (77). The same region is also implicated as a relay centre between emotional regulation and complex body function control. Functional brain imaging studies have demonstrated abnormalities in this region in patients with functional disorders, suggesting that these patients might have an abnormal affective representation of self-relevant information encoded in this region (78) (79). Whether alterations in medial PFC activity represent a common biological abnormality for FNDs and urinary retention requires to be further explored.

It is possible that in some cases, urinary retention may be a manifestation of a functional disorder. However there are a number of gaps in our understanding of chronic idiopathic urinary retention in women, and with the availability of advanced urological and neurological diagnostic tools for investigating the cause for urinary retention, as well as an enhanced understanding of behavioural disorders and FNDs, further research is

needed to explore possible causal associations. Multi-centric cross-sectional and longitudinal studies of women with idiopathic urinary retention undergoing a comprehensive assessment of psychological and functional co-morbidities are needed to answer the following inter-related research questions:

- 1. In some cases, can urinary retention be a manifestation of a functional disorder?
- 2. What is the prevalence of different psychological co-morbidities and functional disorders in women with idiopathic urinary retention? Does this differ from other idiopathic LUT disorders such as OAB?
- 3. Amongst women with idiopathic urinary retention, are there differences in patient characteristics between those with FNDs and those without?
- 4. What is the relationship between chronic stress response and developing urinary retention in humans? Can physical or sexual abuse trigger a stress response culminating in urinary retention?

- 5. Is voiding postponement in the context of oppositional defiance disorder in childhood a risk factor for developing urinary retention in later life?
- 6. In women with idiopathic urinary retention undergoing sacral neuromodulation-
 - Do the outcomes differ in women who have psychological comorbidities and functional disorders?
 - Do psychological co-morbidities and functional disorders improve in women with successful urological outcomes?
- 7. In women with idiopathic urinary retention who are undergoing behavioural therapies for co-existant psychological co-morbidities or functional disorders, do any of these therapies ameliorate voiding dysfunction?

Conclusion: From the available evidence, psychological and functional disorder co-morbidities often co-occur in women with chronic idiopathic urinary retention. The nature of the association between urinary retention and functional neurological disorder co-morbidities needs to be further explored in terms of a disorder of bladder-brain interaction.

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Table 1. Commonly-used screening tools for psychological / psychiatric morbidity in adults (adapted from The Improving Access to Psychological therapies (IAPT) Manual (13)).

Measures / questionnaire	Domains covered	Items
PHQ-9 (14)	Depression	9 items
GAD-7 (15)	Anxiety	7 items
Social Phobia	Social phobia	17 items
Inventory (SPIN) (16)		4
Impact of Events	PTSD	22 items
Scale-Revised (IES-R)		
(24)		
Agoraphobia-Mobility	Agoraphobia	Qualitative (places
Inventory (17)		avoided)

Obsessive-	OCD	42 items
Compulsive Inventory		
(OCI) (18)		
Panic Disorder	Panic disorder	7 items
Severity Scale (PDSS)		
(19)		
Patient Health	Physical	15 items
Questionnaire	symptoms	
(Physical symptoms)	(somatic	
(PHQ-15) (20)	symptoms)	
Francis Irritable Bowel	IBS	5 items
Scale (21)	100	
	7.	
The Chalder Fatigue	Chronic Fatigue	11 items
Scale (22)	Syndrome	7
Work & Social	Impairment in daily	5 items
Adjustment Scale	functioning	
(WASA) (23)		

Table 2. Psychological co-morbidities and functional disorders reported in women with chronic idiopathic urinary retention

Study, number of patients	Co-morbidities reported
de Ridder et al. 2007 (4)	Somatization n=22
n=62	Depression n=15
Everaert et al. 2000 (6)	"hysteria" n=22
n=38	Depression n=6
Hoeritzauer et al. 2016 (10)	Psychological disorders
n=62	Anxiety/depression n=18
	Obsessive compulsive
	symptoms n=3
	Functional Disorders
	-Functional neurological
	symptoms: loss of
	consciousness (n=7), limb
	weakness (n=6), sensory
	disturbances (n=6), memory
	impairment (n=3)

-Unexplained	chronic	pain
syndromes (n=	31)	
		-Unexplained chronic syndromes (n=31)



Table 3. "Urinary Retention" appearing in the Diagnostic and Statistical Manual (DSM)

	Somatization disorders	Conversion Disorders
DSM-III-R	Symptom Groups include	(or hysterical neurosis,
(61)	group of 'Conversion or	conversion type).
	pseudoneurologic	UR not specifically
	symptoms'.	mentioned.
	UR is specifically	
	mentioned as an example	
	of 'conversion or	
	pseudoneurologic	
	symptoms'	
DSM-IV-TR	UR is specifically	UR is specifically
(62)	mentioned as an example	mentioned as an
	of a 'pseudoneurological	example of a symptom of
	symptom'.	conversion disorder

UR: urinary retention

Table 4. Historical cases of urinary retention treated with therapies targeting presumed psychological mechanisms

Reference	Summary	Treatment/ outcome
Williams and	Case report	Psychotherapy-
Johnson (52)	(female); UR	enabled expression
	caused by	of anger
	'emotional conflicts'	Outcome: successful
	after emotional and	Catoonio. Gaocecorai
	sexual abuse	
Chapman (64)	Case study	Psychotherapy-
	(female); childhood	subsequent
	trauma. Patient	enhanced
	unassertive and	confidence and
	exploited by family	assertiveness
		2
		Outcome: successful
Larson et al.(65)	Case study in series	Psychotherapy-
	of 37 women with	enabled expression
	UR and other	of hatred and rage
	symptoms.	towards therapist or
	Diagnosis: schizo-	other male
	affective disorder.	

		physicians
		Outcome:
		successful. UR
		improved although
		some other
		symptoms remained
Wahl and Golden	UR (5 female, 1	Psychotherapy and
(66)	male); Multiple	psychoeducation
	"repressed, genital	Outcome: successful
	sexual conflicts"	Outcome: succession
Cooper (67)	Case report	Reassurance,
	(female)	psychoeducation and
		carbachol injection
	C	followed by injections
		of sterile water
		Outcome: successful.
		UR improved at 4
		months follow-up
Barnard et al. (68)	Case report	Treatment: electrical
	(female)	stimulus to legs and
		programme 'of verbal

		and non-verbal
		reinforcement'
		suggestive of
		assertiveness
		training
		Outcome:
		successful. UR
		cured; less
		dependent and
		anxious; more
		assertive
Barrett (69)	9/12 patients with	Bladder training,
	UR sent for	intermittent self-
	psychiatric	catheterisation and,
	evaluation	when indicated,
		additional 'psychiatric
		support'.
		Outcome: 10
		patients voiding
		normally at discharge

Montague	and	6 patients	Management and
Jones (70)			treatment included
			biofeedback,
			behaviour therapy,
			individual
			psychotherapy, group
			therapy, couples
			therapy, biofeedback-
			monitored relaxation
			training, introduction
			of 'imagery' during
		72	periods of deep
			relaxation.
			Outcome: successful
Bird (71)		2 cases (females)	Analytical
			psychotherapy
			-enabled to express
			ʻunacceptable
			aggressive rage'
			Outcome: successful

Wheeler et al. (72)	12 w	omen with UR	Туре	of
	with	psychological	psychotherapy	not
	histor	у	reported.	
			Outcomes:	not
			reported	

UR: urinary retention

