

Multi-methodological approaches to investigate lower urinary tract function in health and disease

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CHAPTER 9

Valorisation

INTRODUCTION

Lower urinary tract (LUT) dysfunctions are highly prevalent [1], significantly reduce the quality of life of affected individuals [2], and cause an enormous burden on healthcare system and society [3]. In individuals with an underlying neurological disorder, such as spinal cord injury (SCI) or MS, LUT dysfunction are labelled as neurogenic, i.e. NLUTD and pose a long-term threat to the upper urinary tract (UUT) [4]. When NLUTD is improperly managed, affected individuals may establish renal insufficiency or even failure long-term [5, 6]. Furthermore, NLUTD is associated with the development of LUT malignancies, such as bladder cancer [7]. Individuals suffering from SCI are prone to autonomic dysfunctions [8]. As an example, cardiovascular disease as a result of autonomic dysfunction is the leading cause of death in individuals with SCI [8]. In particular, individuals with an injury at or above the spinal segment T6 are at risk to experience autonomic dysreflexia (AD) [9]. The latter is elicited through noxious or innocuous stimuli originating from below the lesion level [9]. The urinary bladder is one of the most frequent causes for AD [10]. This potentially life-threatening situation, characterized by a sudden increase in systolic blood pressure (SPB) >20 mmHg from baseline [9], which can be accompanied with clinical symptoms such as headache, flushing, piloerection, or profound sweating, can result in brain hemorrhage, stroke, or even death [11]. In order to reduce the detrimental long-term effect of LUT dysfunctions in individuals with and without underlying neurological disorder, appropriate assessments, treatment and follow-up strategies must be established. Furthermore, to increase the beneficial effect of currently available treatment options or to develop novel therapeutics, we need to expand our knowledge about supraspinal LUT control.

ASSESSMENTS

To find out whether the LUT is functioning properly or not, several assessments are available (and should be performed). Obtaining past and present medical history including bowel, sexual, and neurological history are highly recommended [4]. Furthermore, bladder diaries, specific questionnaires on patient's quality of life (QoL) as well as urinary, bowel, sexual, and neurological symptoms provide excellent information [4]. A thorough physical examination should include the palpation of genital and reproductive organs as well as a neuro-urologic status. The latter comprises the assessment of sensations and reflexes of the spinal segments Th10 to S5 [4]. Diagnostic procedures, such as urinalysis, blood chemistry, free uroflowmetry, urinary tract imaging (e.g. ultrasound) are well-established in daily practise of urologists [4]. Invasive diagnostic tools such as urethro-cystoscopy and urodynamic investigation (UDI), are used to identify LUT dysfunctions worldwide. The combination of both will allow one to detect anatomical and functional changes of LUT.

OUTCOME

The results of our studies provided new insights on healthy subjects and patients with NLUTD alike, as we were able to answer specific research questions. For the clinical research studies 1 to 3 (Chapters 2 to 4), we utilized recommended assessment strategies. As such, urethro-cystoscopy (Chapter 2) revealed the presence of muscle-invasive bladder cancer and other (partially premalignant) changes of the bladder mucosa in patients with NLUTD. Furthermore, we detected more than 70% of our female SCI patients are exposed to autonomic dysreflexia during UDI (Chapter 3) and provided evidence that UDI is not a valid instrument to identify "healthy" subjects (as 70% of the "normal controls" had pathological UDI findings).

With regards to our experimental studies 4 to 6 (Chapters 5 to 7), we successfully implemented the assessment of structural and functional magnetic resonance imaging according to our study protocols (Chapter 5 and 6) while utilizing our novel infusion-drainage device (Chapter 7) at a high system accuracy to elicit supraspinal activity in interoceptive and LUT control areas.

IMPACT ON ONGOING WORK

Given our results from Chapter 3 and the well-known potential health risk involved with AD, we continued to investigate individuals with SCI in order to find predictors for AD during UDI. We were successful and revealed two significant independent predictors, i.e. level of SCI and presence of neurogenic detrusor overactivity. This study, which is currently under consideration for publication, will help urologist to take better care of individuals with SCI, but most importantly to protect patient who are at the highest risk for AD when assessing LUT function during UDI. With the positive experience from our experimental study designs (Chapter 5 and 7), we were able to successfully investigate task-specific supraspinal activity related to LUT stimulations. First, we could provide evidence for the repeatability of supraspinal activity in healthy subjects [12]. In addition, we revealed differences in supraspinal activity related to LUT stimulations between healthy subject and individuals with 1) non-neurogenic overactive bladder [13] and 2) spinal cord injury [14]. Furthermore, we found differences in supraspinal activity related to LUT stimulation in healthy subjected when using body warm and cold saline [15].

OUTLOOK

In light of the promising results from our experimental studies, presented in this thesis and the previous section related to ongoing research, we feel con-

confident to find significant changes in supraspinal activity related as an indicator for efficacy of treatment, which has been applied to improve LUT function in individuals with either LUT dysfunction or NLUTD. Furthermore, we are confident to find a significant beneficial effect of NLUTD treatment, such as onabotulinumtoxinA or fesoterodine, to reduce frequency and severity of AD, and to improve LUT and cardiovascular function as well as quality of life in individuals with SCI.

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