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CAN MODELLED ANALYSIS OF PRESSURE-FLOW STUDIES GIVE INFORMATION ON THE EFFERENT NERVOUS ACTIVITY IN BOTH BLADDER AND URETHRA DURING MICTURITION?

Hypothesis / aims of study

Each year, physiological studies on men and animals bring new results on the neuronal system, mainly the afferent pathways, governing bladder and urethra. Our objective was, using an extended VBN mathematical model of micturition to analyze pressure-flow studies (PFs), to search for information on the nervous efferent activity during the 3 phases of micturition (continence, voiding, return to continence) in both bladder and urethra.

Study design, materials and methods

Definitions: A modulating force factor □**det(t)** has been introduced to modulate the Griffiths'law f(V,Q) which gives the contractile part of the detrusor pressure, then p_{det}=□(t)* f(V,Q)); in a similar way, □**sph(t)** acts on the sphincter pressure. Let **E(t)** be the calcium effective concentration in the muscular cell [1], □□□□ the ratio of effective regulatory proteins □[1], and □**(t)** = **F**/$\mathbf{F_{max}}$ (**F**=mean efferent nerve firing rate) the efferent nerve activity.

The mathematical model: An extended version of the VBN® model [2] was used for modelled analysis of the recordings. It included a sequence of the physiological phenomena above defined:

$$\zeta(t) \rightarrow E(t) = \frac{E_{max}}{T}\int_{\theta=0}^{\theta=t}\zeta(\theta) * \exp\left(\frac{\theta - t}{T}\right) * d\theta \rightarrow \phi = \left(\frac{E^2}{(1+E)(3+E)}\right)^2 \rightarrow \eta = \frac{5\phi}{4\phi + 1}$$

Computation was made using the reverse sequence starting from □**det(t)** given by $p_{det}(t)$ and from □**sph**=1 during continence (normal case □**sph**=0 during voiding).

The database: It comprised of urodynamic recordings obtained from 71 men [24-86 y] complaining of lower urinary tract symptoms due to benign prostatic enlargement and from 102 women [24-86 y] with urinary incontinence (all types). A total of 112 PFs of men and 147 PFs of women were analyzed. Exclusion criteria were neurological disease, diabetes mellitus, grade > 2 pelvic organ prolapse.

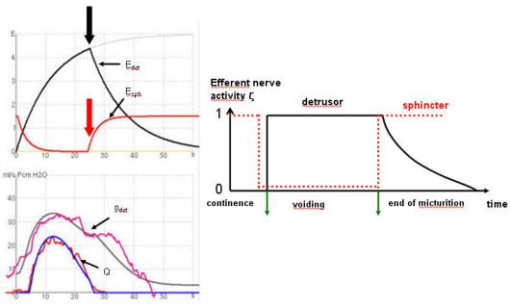
Results

1) For each PFs a set of coherent parameters (obstruction, detrusor contractility…) was found leading to computed tracings fitting well the recorded ones.

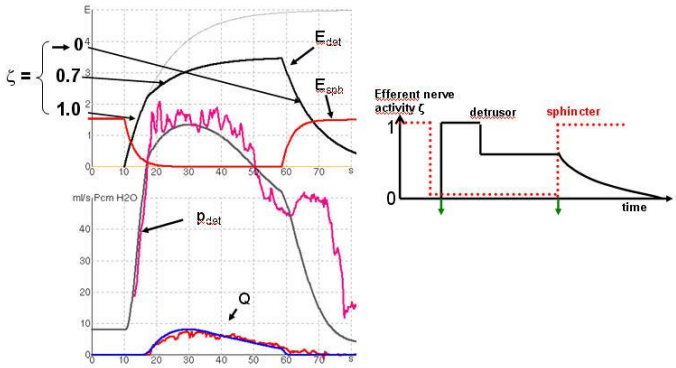
2) The time constant **T** of the efferent signal leading to the free sarcoplasmic Ca^{2+} concentration was identified for the detrusor: $\mathbf{T_{det}}$**=6 s** and the sphincter: $\mathbf{T_{sph}}$**=3 s**.

3) The main result was that the efferent nerves firing rate was a sequence of constant values and both excitations of the detrusor $\mathbf{E_{det}}$**(t)** and of the striated sphincter $\mathbf{E_{sph}}$**(t)** a sequence of exponential functions of time.

a) *The simplest type of micturition:* The last phase (return to continence) began (arrows) when the bladder volume **V** reached a critical value $\mathbf{V_{end}}$ [range 15-50 mL].



b) *The most frequent type of micturition:* Observed in 72% of male and 63% of female PFs. A break of the detrusor excitation occurred at the onset of the voiding phase. A new value of □ was □$_1$ < 1 [range 0.3-0.9]. All the voidings of the same patient had the same □$_1$ value.



4) Return to continence: a) without significant post void residual (PVR): when **V** < 50 mL, $\mathbf{E_{sph}}$ increased exponentially to the storage value with the time constant $\mathbf{T_{sph.end}}$ = 3 s and E_{det} exponentially decreased to 0 with a time constant $\mathbf{T_{det.end}}$ = 11 s. b) for 28 women with large PVR: a break of detrusor excitation occurred 20 s after the onset of flow and return to continence began 40 to 80 s after the break (same time constants) leading to large PVR.

Interpretation of results

Common conditions involve abnormalities of the bladder control. Today, there is a deficient understanding of causes. This analysis shows that modelling can give some insight on the control. Thus, in all computations, we found an unexpected result: the efferent nerve activity □(t) during voiding was a sequence of constant values with brisk changes. In the most frequent type of micturition the □□□sequence can be explained by 2 successive excitatory mechanisms: a triggering signal probably sent by the pons M center followed by the well known positive bladder-bladder feedback. In case of large PVR, the late excitation break could be due to recurrent inhibition or to fatigue.

Concluding message

Animal studies have described some reflexes during the micturition course, but their relative physiological weights are still unknown. Functional imagery of the brain in human [3] has shown what are the specific brain areas working during filling and a general map of the main connecting pathways is suggested, but at a scale which does not allow to follow the signal processing. On the contrary, the analysis of recordings of PFs gives some light on the signal processing, but is not concerned by brain localizations. Thus, the method described in this study appears as a complement to the previous ones.

References

1. Kybernetes 1985; 14: 241-251.
2. NAU 2000; 19:153-176.
3. NAU 2008; 27: 466-474.

Specify source of funding or grant	**None**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require ethics committee approval because	**It involved retrospective analysisof urodynamic studies from a database.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**No**