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FORCED DIURESIS AS A TOOL FOR THE NON-INVASIVELY EVALUATION OF BLADDER SENSATION

Hypothesis / aims of study
Currently, the only method to evaluate the development of bladder sensation is cystometric bladder filling, which is unfortunately an invasive investigation. Bladder diaries that provide a sensation grading scale with every void are used to evaluate bladder sensation non-invasively. However, it only gives information on the perceived sensation that an individual has before he goes to the toilet and summarises the voiding data for several days. It does not provide information at which volume sensation develops and how it evolves during further filling. This study describes a new non-invasive method to study the origin and development of bladder filling sensation and evaluates the repeatability of the method.

Study design, materials and methods
Eleven healthy volunteers participated in the study. To ensure a constant high diuresis a strict water loading protocol was given to all. One hour before the start of the protocol they were asked to drink 1000mL of water. The water loading was continued during the whole protocol by asking them to drink another 200mL every 10 minutes, with a maximum of an extra 1000mL during the protocol. To evaluate bladder sensation they were asked to grade their bladder sensation every ten minutes and also whenever they noticed any change. Gradation of the bladder sensation was done by giving the participants an empty graph. The X-axis was an open end time scale and the Y-axis graded intensity of sensation starting from 0 (empty bladder) to 100% (absolute need to go to void). To reduce any bias in interpretation, we deliberately did not provide any terms or description for the sensations. The protocol ended when the participants indicated an absolute need to go to void. At that timepoint they were allowed to void and the voided volume was measured. This protocol was conducted three times with 10 days interval.The data are expressed as “intensity of sensation” (percentage of the maximum intensity representing the sensation of the need to void) and volume, accepting a constant diuresis throughout the protocol.

Results
The forced diuresis (mean: 12.1 ± 3.4 mL/min; range: 4.3 – 18.4 mL/min) and duration of a session (mean: 62 ± 12 minutes; range: 38 – 86 min) was not different between the three sessions (Wilcoxon signed rank test with Bonferroni correction repectively was $p>0.12$ and $p>0.17$).
Two patterns of sensation development were found which are shown in figure 1. Type L (L-shape), characterized by two phases and type S (S-shape) characterized by three phases. In both types, phase 1 shows a slowly increasing intensity of sensation and phase 2 a steep rise in sensation intensity. For the L-type pattern, this steep rise (phase 2) leads to an absolute need to void, whereas for type S, a third phase is identified, again characterized by a slowly increasing sensation intensity, finally leading to an absolute need to void. For an individial, the sensation pattern stayed the same for the three sessions (figure 2).
Although no statistical difference ($p>0.06$) was found in the volume at which a first sensation was noted (intensity increasing from zero percent) between the three sessions, there was a large variation within an individual. Mean volumes respectively were 152 ± 174 mL, 231 ± 156 mL and 274 ± 152mL, for the first, second and third session. However the slope of the phase 2, which represents the speed of change in sensation, showed less variation and was not different for the three sessions (mean slope: 0.25 ± 0.12; range: 0.13 – 0.53; Wilcoxon signed rank test with Bonferroni correction all $p> 0.07$). The mean voided volume at the sensation of “absolute need to go to void” was 746 ± 223 mL (range: 240 – 1120 mL) and was not different between the three sessions (Wilcoxon signed rank test with Bonferroni correction all $p> 1.00$).

Interpretation of results
The water loading protocol as used in this study gives a diuresis with a wide inter-individual range, but without a difference intra-individually measured for the different sessions over time. Two different patterns of sensation are noted (L and S type) for the different participants, but the shape is constant intra-individually. Furthermore, the volume at which a sensation is first noted, which is the volume at which sensation increases form zero percent intensity, is not different for the three sessions but appears to be the part of the curve that is the most variable of the sensation curve. The rate of sensation intensity change over the second phase appears to be constant leading to a voided volume at the sensation of an absolute need to go to void, which is constant over the three sessions.

Concluding message
A strict water loading protocol can induce a constant forced diuresis, which can be used as tool to study the origin and development of bladder filling sensation in non-invasive way. This study shows that in healthy volunteers two patterns exist, which can be reproduced by the proposed protocol. This technique may help to understand the basics behind the development of normal bladder sensation and can then be used as a guide to understand how sensation develops in pathological conditions such as the overactive bladder syndrome.

Figure 1 Shows the two types of patterns, the L shape and the S shape.

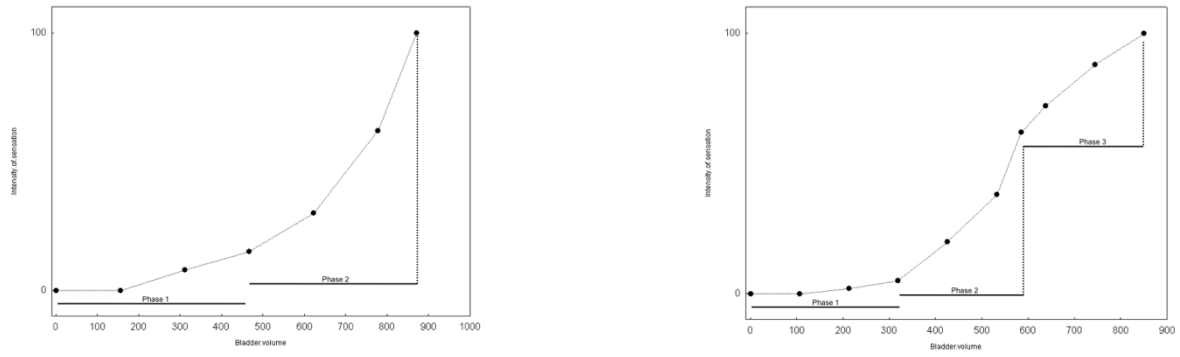
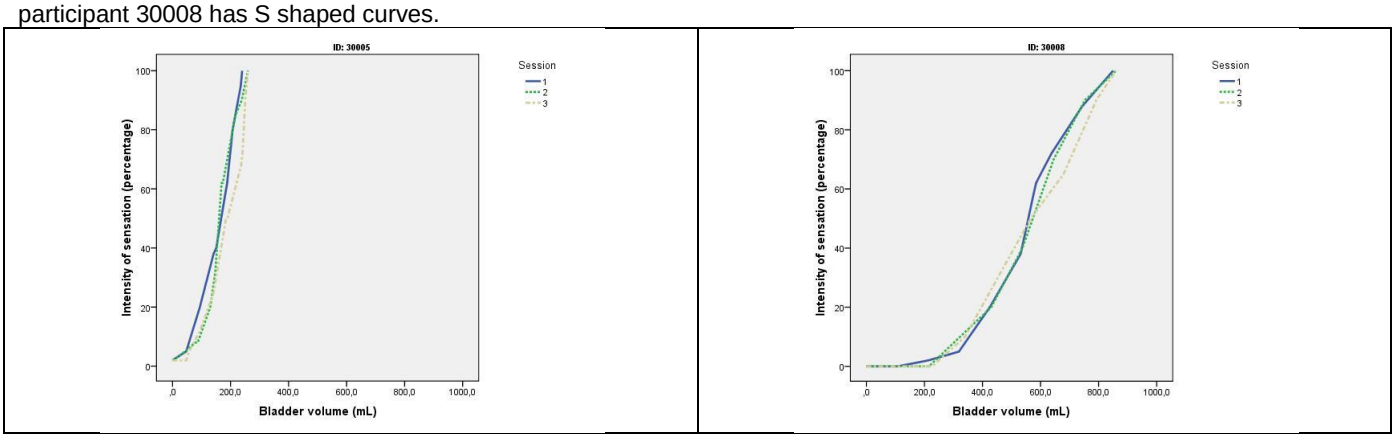


Figure 2 Shows the curves for all sessions for 2 different participants. The curves for participant 30005 have a L shape while participant 30008 has S shaped curves.



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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Medical Ethical Committee Maastricht University Medical Centre**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**