

## Effects of different degrees of bladder distension on nociceptive withdrawal reflex in healthy subjects.

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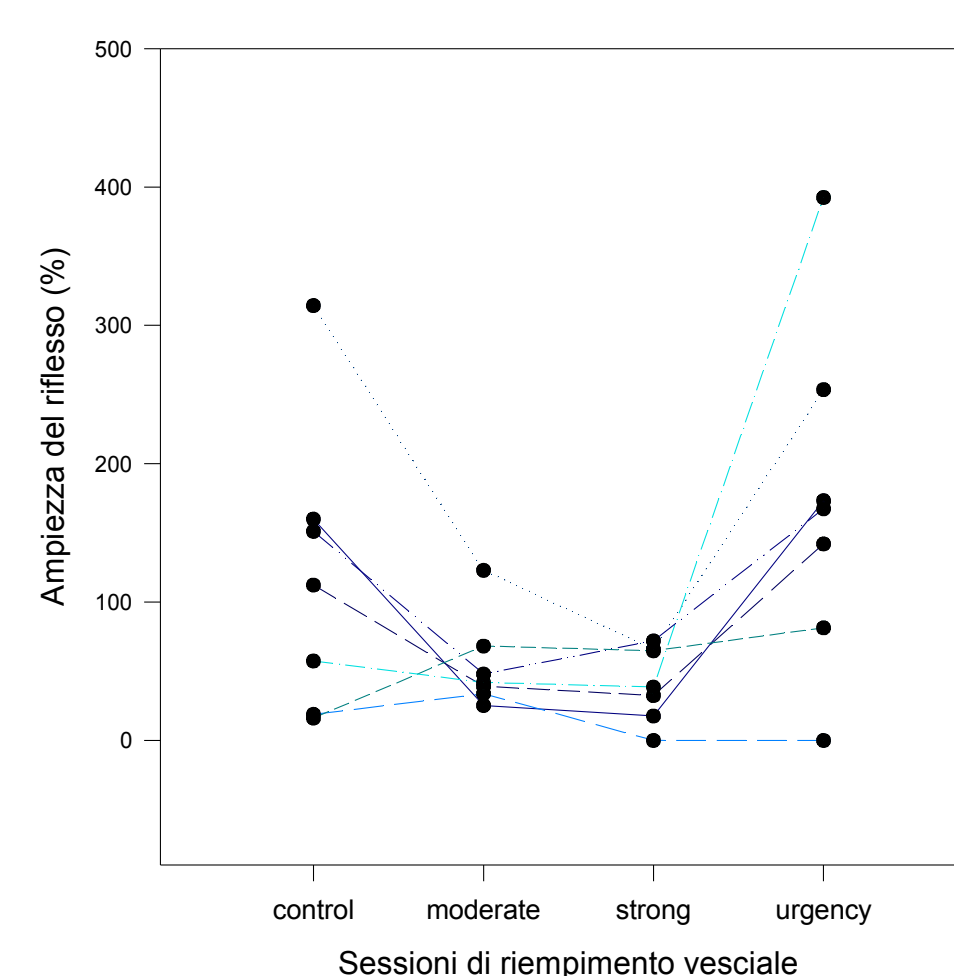
**Introduction:** Viscerosomatic convergence of nociceptive information is a neural phenomenon well documented in experimental studies and it is considered the primary mechanism underlying referred pain. It is known that progressive distensions of the bladder can inhibit the magnitude of the nociceptive withdrawal reflex (NWR) and its related individuals' pain sensation in healthy subjects. A central role for the periaqueductal gray (PAG) as the main centre of functional connectivity between bladder afferents during storage and nociception control may be hypothesized (1). More recently higher levels of bladder distensions (urgency sensation) have shown to produce a decrease in the NWR amplitude in the upper limbs, whereas a similar decrease has not been found in the lower limbs suggesting that excitatory nociceptive inputs from bladder afferents counterbalance the descending inhibitory effect on sacral spinal cord (2). To clarify the effects of bladder distension on the NWR, we studied the reflex in both upper and lower limbs during 4 different degrees of bladder filling.

**Results and Discussion:** A significant effect of bladder distension was found on NWR amplitude in both lower and upper limbs (Chi square = 10.565,  $p=0.014$ ) with higher values during the urgency session compared to both moderate and strong sessions in the lower limbs and with lower values during moderate and urgency session compared to the control session in the upper limbs. A significant effect of bladder distension was found on NRS scores in upper limbs but not in the lower limbs ( $p>0.05$ ).

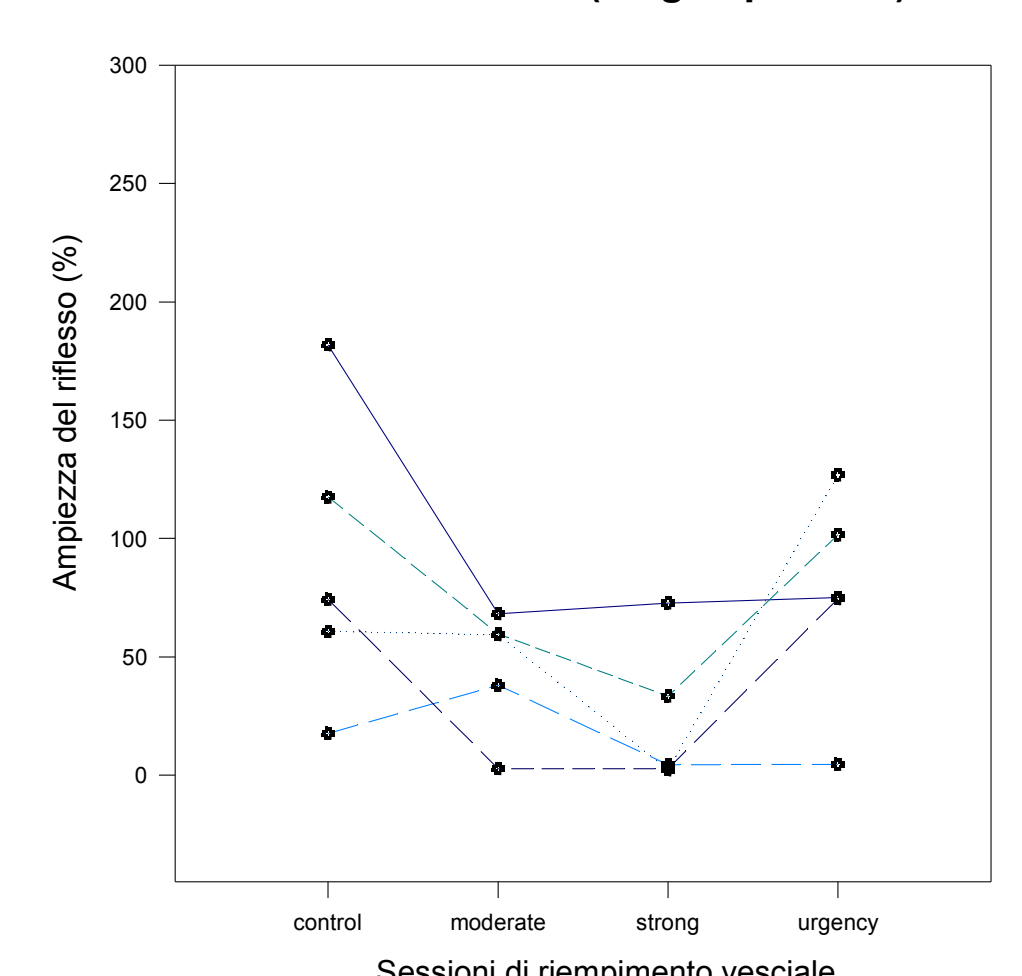
It is known that high level bladder distension activates through A-delta and C afferents, excitatory sacral spinal interneurons, namely WDR neurons and simultaneously activates inhibitory supraspinal pathways, i.e. PAG, which in turn inhibits thoroughly both spinal cord interneurons and motoneurons (1). The present study confirms that bladder filling activates descending antinociceptive pathways but, at maximum level of bladder distension (urgency), excitatory bladder afferents counteract the inhibitory effect of descending pathways with a prevalence of excitation at sacral level.

**Materials and Method:** NWR amplitude and NWR pain-related perception were recorded in both lower and upper limbs in 7 healthy volunteers (3 men and 4 women, mean age  $28 \pm 5.9$ ), during 4 recording sessions: empty bladder (baseline session), moderate bladder filling (moderate desire session), high bladder filling (strong desire session) and maximum bladder filling (urgency session). Participants were instructed by the investigator to drink 1-2 liters of water and hold their urine until instructed otherwise. Bladder filling was evaluated with suprapubic bladder sonography. NWR was evoked by stimulating the sural nerve in the lower limb and the index finger digital nerve in the upper limb (figures 1,2). NWR pain-related perception was quantified on a 10-point pain scale (NRS). Repeated measures ANOVA on rank was used to evaluate the effect of bladder filling on NWR amplitude. NWR amplitude has been reported as mean  $\pm$  standard error of the mean (SEM).

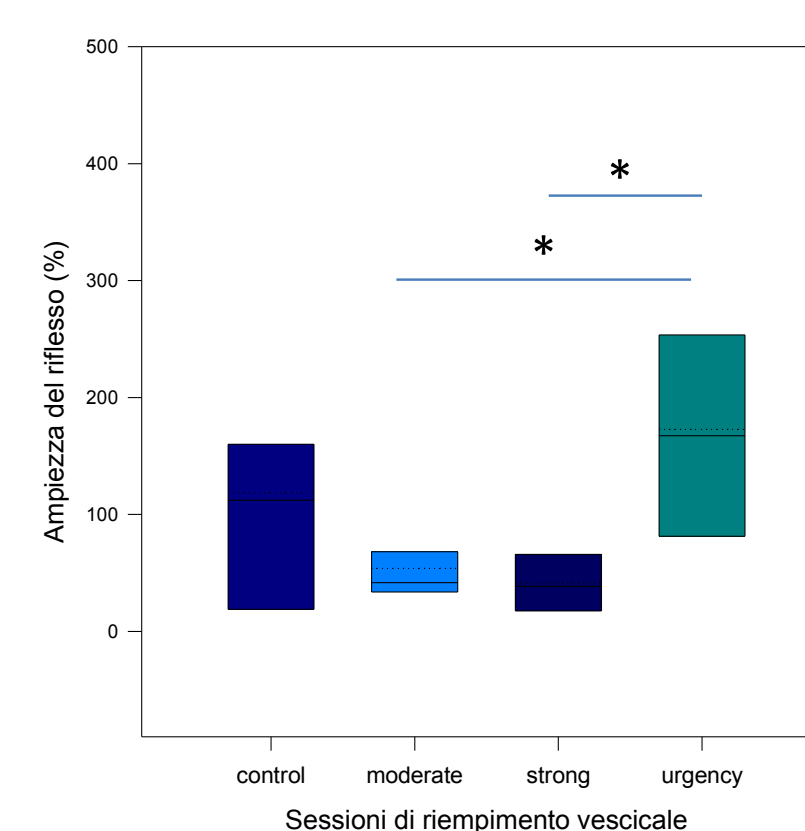
Effetto del riempimento vescicale sull'ampiezza del riflesso nocicettivo (singoli pazienti) AAL



Effetto del riempimento vescicale sull'ampiezza del riflesso nocicettivo (singoli pazienti) AAS



Effetto del riempimento vescicale sull'ampiezza del riflesso nocicettivo (medie) AAL



Effetto del riempimento vescicale sull'ampiezza del riflesso nocicettivo (medie) AAS

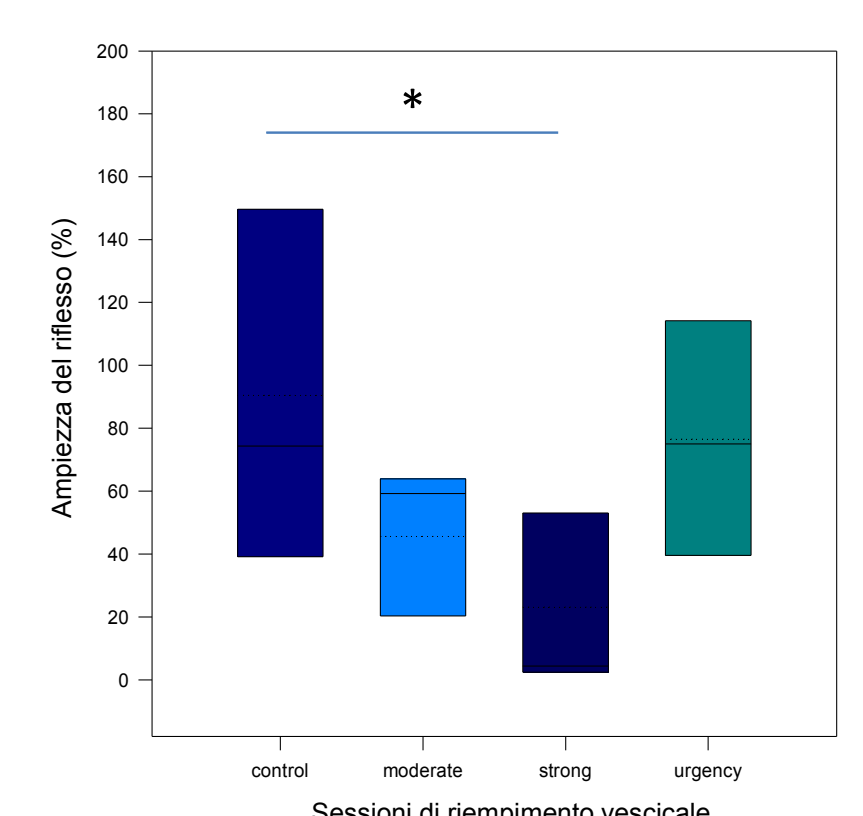


Figure 1. Example of NWR recording in both upper and lower limbs during the four sessions.

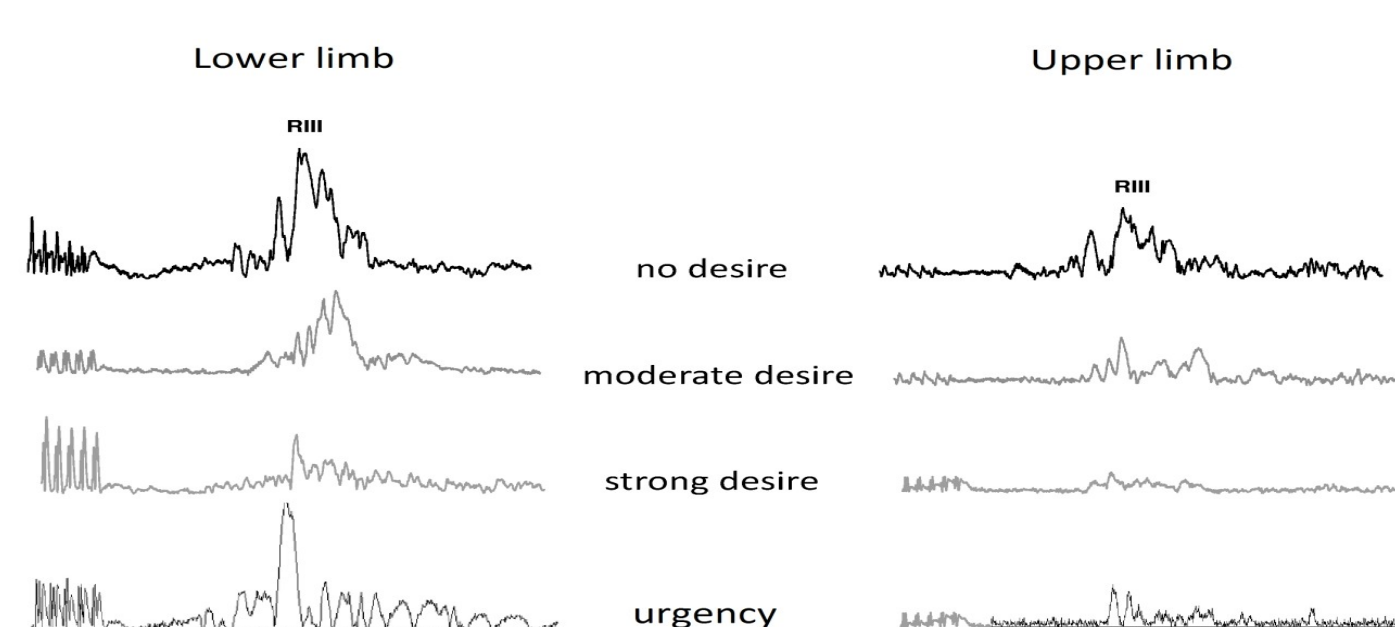
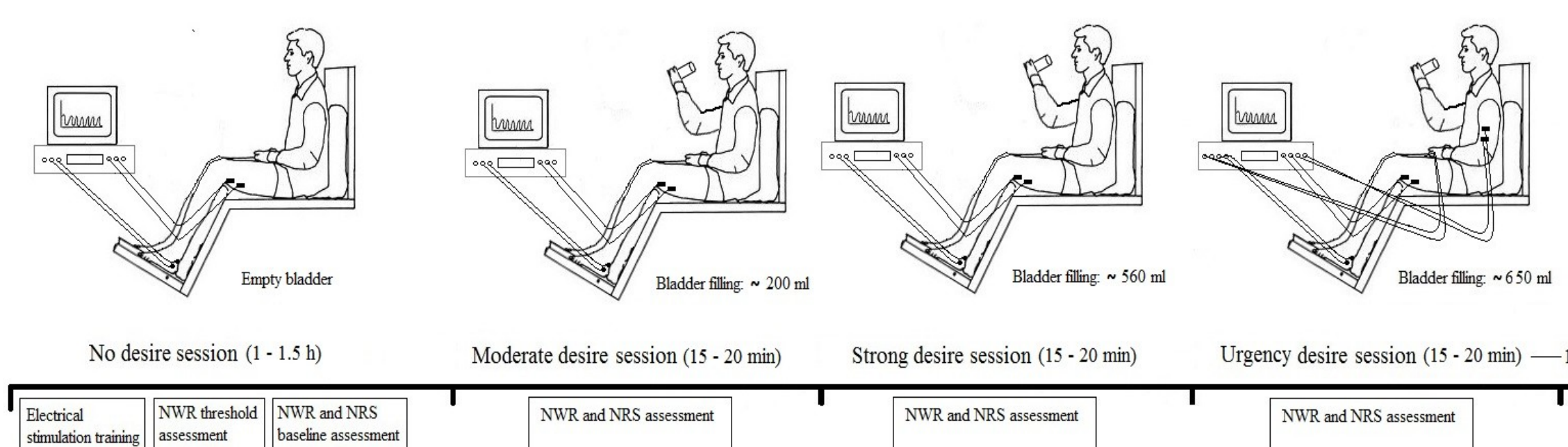


Figure 2. Experimental setup.



**Conclusions:** The effect of bladder filling on NWR may represent a useful tool to investigate the viscerosomatic interaction between bladder afferents and somatic nociception. A better understanding of this interaction in healthy subjects could provide useful information about bladder training in patients affected by various neurological diseases.

### References:

- 1) Serrao M, Cortese F, Fragiotta G, Pastore AL, Palleschi G, Coppola G, Carbone A, Pierelli F. Bladder filling attenuates spinal cord nociceptive reflexes in humans. *Clin Neurophysiol* (2014); 125(11):2271-6.
- 2) Fragiotta G, Cortese F, Coppola G, Carbone A, Pastore AL, Palleschi G, Mastroianni S, Conte C, Perrotta A, Pierelli F, Serrao M. Effect of high level of bladder filling on spinal nociception and motoneuronal excitability. *Exp Brain Res* 2015 DOI 10.1007/s00221-015-4416-4.