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NEURAL MECHANISMS OF TONIC AND PHASIC URETHRAL CONTINENCE REFLEXES PREVENTING STRESS URINARY INCONTINENCE

Hypothesis / aims of study

The aim of this study is to clarify urinary continence mechanisms during two different stress conditions in rats in order to elucidate the role of active urethral closure function in preventing stress urinary incontinence (SUI) using rats. The urethra consists of proximal smooth muscle and mid urethral striated muscle components with different innervations and different neurotransmitters. Therefore, we sought to elucidate which portion of the urethra or which sphincter is more important to protect against SUI to identify possible targets for pharmacotherapy of SUI.

Study design, materials and methods

In adult female rats, urethral contractile responses were measured using micro-tip transducer catheters under urethane anesthesia. Leak point pressure (LPP) defined as intravesical pressure that induced leakage from the urethral orifice was also measured. First, following acute spinal cord transection that prevented reflex bladder contractions, urethral responses and LPP were measured during passive increments in Pves (20-60 cmH2O) for 2 min or during direct bladder compression to evaluate the bladder-to-urethral continence reflexes during Valsalva-like passive Pves elevation. Secondly, the sneeze reflex was induced by a rat whisker inserted into the nostrils to evaluate the sneeze-induced urethral continence reflex using micro-tip transducer catheters and LPP measurements. Then, the effects of bilateral transection of either pelvic nerves, pudendal nerves, nerves to pelvic floor muscles such as ilio/pubococcygeous muscles, or hypogastric nerves on urethral responses during passive Pves elevation were examined to evaluate the contribution of smooth and striated muscle sphincters to stress-induced continence reflexes.

Results

1. Bladder-to-urethral reflexes during Valsalva-like passive Pves elevation

During passive Pves elevation, a restricted portion of the middle to proximal urethra (12.5-15 mm from the urethral orifice) showed Pves-dependent tonic contractile responses that were abolished by cutting the pelvic nerves bilaterally. In pelvic nerve-intact rats, bilateral transection of either hypogastric nerve, pudendal nerve or nerves to ilio/pubococcygeous muscles significantly reduced contractile responses during Pves elevation, and combined transection of these three sets of nerves totally abolished the urethral closing responses. In pelvic nerve-transected rats, LPP was significantly reduced by 30-35% compared with normal rats whose LPP was 50-60 cmH_2O during passive Pves elevation or direct bladder compression.

2. Sneeze-induced urethral reflexes

During sneezing, phasic contractile responses, which were greater than the size of Pves increases, were observed at the middle urethra, but not at other parts of the urethra. These sneeze-induced mid-urethral responses were independent of the strength of sneezing and did not disappear after opening the abdomen. However, pressure responses at the middle urethra during sneeze were negligible when somatic nerves (pudendal nerves and nerves to ilio/pubococcygeous muscles) were transected while transection of pelvic nerves or hypogastric nerve had no effects on sneeze-induced urethral contractile responses. In somatic nerves-transected rats, sneeze LPP was 16.2 ± 2.1 cmH_2O, while no urinary leakage was induced in normal rats during sneeze, which increased Pves to 37 ± 2.2 cm H_2O.

Interpretation of results

These results indicate that urethral continence mechanism has two distinct components. Tonic urethral continence mechanisms during Valsalva-like passive Pves elevation that activate afferent pathways in the pelvic nerve is mediated by contractions of proximal-to-middle smooth/striated muscles and pelvic floor muscles induced by efferent pathways such as sympathetic adrenergic nerves in the hypogastric nerve and somatic nerves in the pudendal nerve and nerves to pelvic floor muscles. The additional phasic response during

sneezing is mediated by mid urethral striated muscles and pelvic floor striated muscles via activation of somatic nerves (pudendal nerve and nerves to pelvic floor muscles), but not via sympathetic nerves.

Concluding message

It is assumed that Pves-induced bladder-to-urethral continence reflexes can be activated during tonic abdominal pressure rises induced by Valsalva-like stress conditions such as laughing, jogging or lifting heavy objects, and that another continence mechanism can be activated by even stronger, phasic stress conditions such as sneezing or coughing. Therefore, pharmacotherapy that can increase striated muscle sphincter function to enhance both phasic and tonic continence reflexes might be more clinically useful to treat SUI than the therapy targeting the smooth muscle sphincter, which seems to be involved only in the tonic continence reflex.

FUNDING: National Institutes of Health DK067226