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Dobberfuhl A D[1], Chen B[2], Han X[1], Diaz E C[1], Comiter C[1]
1. *Stanford University, Dept. of Urology,* ***2.*** *Stanford University, Dept. of Obstetrics and Gynecology*

PERFORMANCE VALIDATION OF AN AUTONOMOUS 12-CHANNEL 100-GRAM LOAD CELL SENSOR ARRAY FOR THE LONGITUDINAL ASSESSMENT OF RAT BLADDER FUNCTION

Hypothesis / aims of study: The metabolic cage is an important non-invasive tool used to assess ambulatory voiding function in conscious rodents. Other standardized assessments of lower urinary tract (LUT) function in the rat include the 2-hour filter paper test and bladder cystometry, however these tests are labor intensive and represent a single point in time. We sought to validate our enhanced metabolic cage with a novel 12-channel 100-gram load cell sensor array, which allows for the autonomous assessment of LUT function longitudinally over time. The aim of our study is to validate the performance and reliability of our sensor array against the 2-hour filter paper test and anesthetized bladder cystometry.

Study design, materials and methods: LUT function of female Sprague-Dawley rats were assessed at multiple time points with: A) 2-hour filter paper test (n=35, 129 samples), B) Metabolic cage (n=35, 129 cage cycles) and C) Anesthetized bladder cystometry (n=6). Twelve rats were simultaneously housed in metabolic cages (Tecniplast, Model 3701M081) during each cage cycle (18 to 24 hours). For the first 2-hours of each cage cycle, voided volume was measured by calculating the area of each urine droplet on filter paper. Voided volume for each animal was then measured using twelve 100-gram Wheatstone bridge load cells (sensitivity 50 uL) connected to three 4-channel bridge amplifier USB transducers (Phidgets Inc., Model 1046) and data recorded continuously at 1-second intervals (DSP Robotics, FlowBotics Studio v3.0.8). Anesthetized cystometry was then performed (urethane, 1.2 g/kg). Data analysis was performed in SAS Studio (Cary, NC, USA) using ANOVA, Pearson correlation and generalized linear regression.

Results: Load cell sensor performance was assessed for all 12 sensors simultaneously (14 droplets each from 100 to 3,000 uL) to simulate voided volume. Direct sensor calibration using a micropipette demonstrated accurate correlation with known droplet weight ($r = 0.998$, $p<0.001$; sensitivity range 100 to 3,000 uL). Accurate correlation with known droplet weight was also noted with droplet passage through clean ($r = 0.995$, $p<0.001$; sensitivity range 200 to 3,000 uL) and dirty metabolic cages. Metabolic cage nocturnal mean voided volume (n=35, 129 cage cycles) significantly correlated with the number of voids ($r = -0.45$, $p<0.001$ and $r = -0.54$, $p<0.001$), void interval ($r = 0.68$, $p<0.001$ and $r = 0.61$, $p<0.001$) and maximum voided volume ($r = 0.74$, $p<0.001$ and $r=0.92$, $p<0.001$) for both day and night respectively. The 2-hour filter paper test demonstrated voided urine droplet volumes which closely correlated ($r = 0.55$, $p<0.001$) with daytime voided volumes obtained by metabolic cage. Nocturnal mean voided volume demonstrated a non-significant (n = 6) positive correlation with cystometric mean voided volume ($r = 0.48$, $p=0.33$), intercontractile interval ($r = 0.65$, $p=0.16$) and mean threshold pressure immediately prior to productive void ($r = -0.27$, $p=0.60$). Nocturnal mean voided volume was consistently greater in ambulatory conscious rats (mean 1,014 uL, range 577 to 2,223 uL) compared to anesthetized cystometry (mean 126 uL, range 20 to 211 uL). A positive non-significant trend was noted for correlation between cystometric intercontractile interval and ambulatory interval between voids in conscious awake rats, with the strongest correlation ($r = 0.59$, $p=0.22$) noted during the nocturnal phase of voiding.

Interpretation of results: Metabolic cage assessment of LUT function correlated with voided volumes using the filter paper test and anesthetized bladder cystometry. Rat bladder function and behavior patterns may be reliably assessed over time with our enhanced metabolic cage, without the need for anesthesia or terminal bladder cystometry.

Concluding message: The basic metabolic cage equipped with a 100-gram load cell sensor array can reliably and longitudinally assess rat bladder function over time.

Disclosures
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