

## **CENTRALLY-MEDIATED CHANGES IN URODYNAMIC PARAMETERS DURING SLOW WAVE SLEEP**

### Hypothesis / aims of study

Micturition does not normally occur during sleep. This is due in part to absence of fluid intake, the diurnal increase in antidiuretic hormone and circadian change in intrinsic bladder compliance. In addition, it is possible that there are central effects on bladder function due to dynamic changes in brain state.

The general anaesthetic urethane promotes a condition of behavioural unconsciousness that closely mimics the full spectrum of natural sleep. The electroencephalogram (EEG) shows spontaneous and rhythmic changes in brain state that resemble slow wave, and rapid eye movement sleep (REM)-like brain sleep states with a period of around 11min (1). We used the urethane-anaesthetised rat preparation as a model system to facilitate mechanistic studies into changes in urodynamic parameters during continuous cystometry in sleep-like brain states.

### Study design, materials and methods

The study conforms with the national guidelines for the care and use of animals and was carried out under the authority of a UK Home Office Project Licence.

Male rats were anaesthetised with urethane (1g Kg<sup>-1</sup> i.p.). They were instrumented to record cortical EEG, blood pressure, heart rate and respiratory airflow. A venous catheter was inserted for infusion of fluids and rectal temperature was maintained at 37°C. Following a midline laparotomy, a canula was inserted through the bladder dome to record vesical pressure and to infuse saline. EMG activity was recorded from the external urethral sphincter (EUS). The time and volume of voids was also measured. EEG state was quantified by measuring the power in the 0.5-1.5Hz bandwidth of the EEG. Continuous cystometry was performed during infusion of saline into the bladder (6ml h<sup>-1</sup>).

### Results

Infusion of saline into the bladder evoked repeated cycles of filling and voiding. During filling, bladder pressure remained low (around 10mm Hg) and continence was maintained by low level of tonic activity in the EUS. Voids were characterised by a sharp rise in bladder pressure. At this time the level of tonic activity in the EUS also increased, before switching abruptly to a bursting pattern (7Hz for 3-5s), during which time fluid was expelled via the penis. Bladder pressure then returned to the pre-voiding level. As the EEG cycled from an activated (low amplitude, high frequency (3-5Hz) state) to a synchronized (high amplitude, low frequency (1Hz) state), there was a pronounced change in urodynamic parameters. The threshold voiding pressure and threshold voiding volume both increased, whilst end-filling compliance decreased (Figs 1 and 2). The rhythm of voiding was also disrupted; voids became more irregular and less efficient, often presenting as double contractions.

### Interpretation of results

The micturition cycle, including the presence of high frequency oscillations of the sphincter during voiding, persists under urethane anaesthesia in a manner similar to that reported previously in unanaesthetised rodents. Spontaneous transitions between EEG states, resembling those of recognized sleep states, were accompanied by alterations in storage compliance and voiding threshold, which promoted urinary continence during slow wave activity that resembled deep sleep.

The data show that centrally-mediated alterations in urodynamic parameters occur during changes in sleep-like brain states in rats. Disruptions of central regulation could be a potential contributory factor in sleep-related urinary dysfunction, such as nocturnal enuresis in humans.

### Concluding message

Transition between sleep states alters urodynamic properties, with clear differences in bladder compliance and voiding threshold between activated and synchronized EEG states.

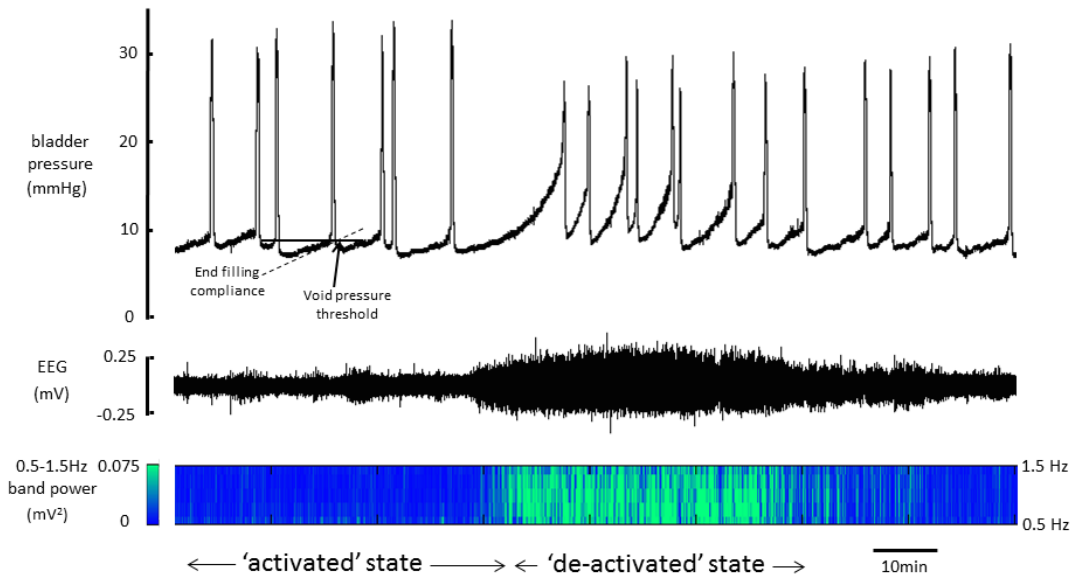


Fig. 1. Urodynamic record during continuous infusion of saline into the bladder ( $6\text{ml h}^{-1}$ ) as EEG cycles from an activated (blue) to deactivated 'slow wave' state (green).

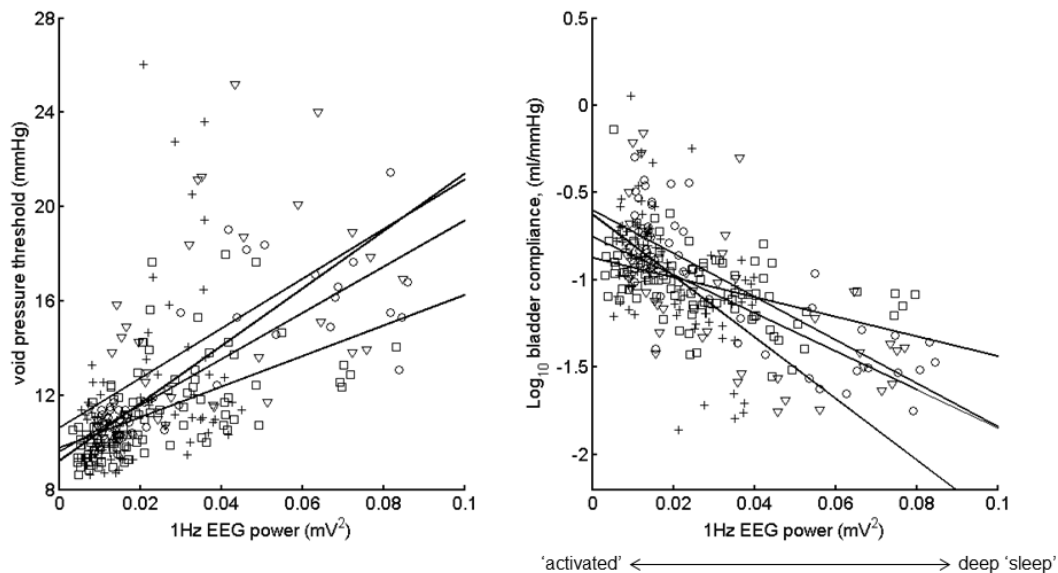


Fig 2. Relationship between EEG power at 0.5-1Hz, voiding threshold pressure and end filling compliance for 4 rat preparations.

#### References

1. Clement EA, Richard A, Thwaites M, Ailon J, Peters S, Dickson CT (2008) Cyclic and sleep-like spontaneous alternations of brain state under urethane anaesthesia. PLoS ONE 3(4): e2004.

#### Disclosures

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