

Modeling dementia-related voiding dysfunction using transgenic Alzheimer disease mice

Jeremy B Tuttle

University of Virginia School of Medicine, USA

Urinary incontinence is the most common cause of institutionalization in dementia. Urinary voiding dysfunction is associated with all forms of dementia, including the most common, Alzheimer disease. This suggests the micturition neural circuitry is affected by the dementia disease process. However, this has never before been examined in an animal model to understand where and how micturition circuits are impacted. Furthermore, the anticholinergic drugs used to aid bladder control have not been studied for possible interactions with the disease processes affecting normal micturition. We have shown previously that oxybutinin and tolterodine, commonly prescribed for bladder control, reduce brain amyloid, plaques and improve cognitive performance in a transgenic mouse (Tg) model of Alzheimer disease (AD). We tracked voiding in these Tg mice, measured amyloid and plaque density in the brain and spinal cord and determined relationships between pathophysiology, cognitive performance and voiding dysfunction. The study was expanded to include another Tg AD line with differing genetic background and transgenes.

Surprisingly, males and females of the two lines differed in the development and persistence of cognitive deficits (elevated plus maze), voiding frequency, awake cystometry, plaque deposition and BACE1 expression. However, the two strains also differed in that females fared better in one whereas males were less affected in the other. The formation of diffuse amyloid plaques in the spinal cord indicates that micturition circuit function may be impacted at brain and spinal levels. These results will be presented and discussed. Supported by NIH/NIA 5RO1AG028636.

Biography

Dr. Tuttle earned the Ph.D from Johns Hopkins University School of Medicine followed by postdoctoral studies at the University of Connecticut. His laboratory has been supported by NIH for over 30 years, as well as foundations and industry. Having authored over 140 published works, he has traveled and lectured extensively in Japan, Europe and North America, served on numerous study sections, editorial boards, has organized symposia and trained many that have gone on to their own distinguished careers. His work spans Neuroscience, Cardiovascular and Urological sciences from molecular through behavioral aspects.

tuttle@virginia.edu