Neural control of the lower urinary tract in health and disease

Jalesh N. Panicker MD, DM, FRCP

Consultant Neurologist and Clinical lead in Uro-Neurology

The National Hospital for Neurology and Neurosurgery

and UCL Institute of Neurology

Queen Square, London

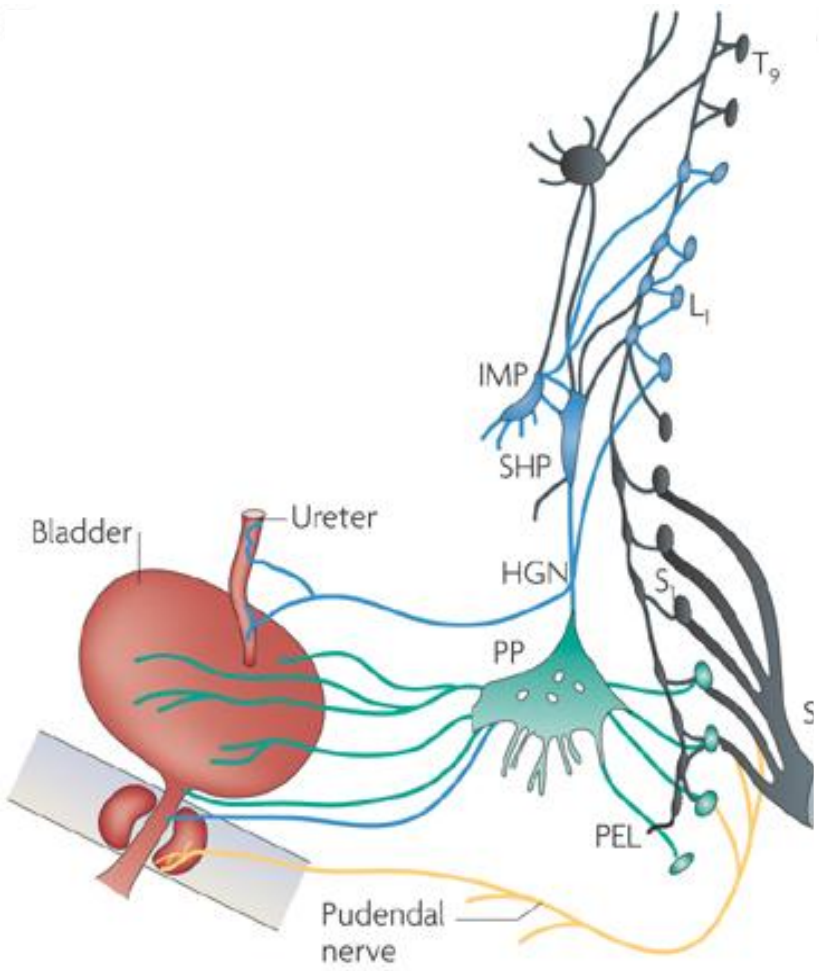
Outline

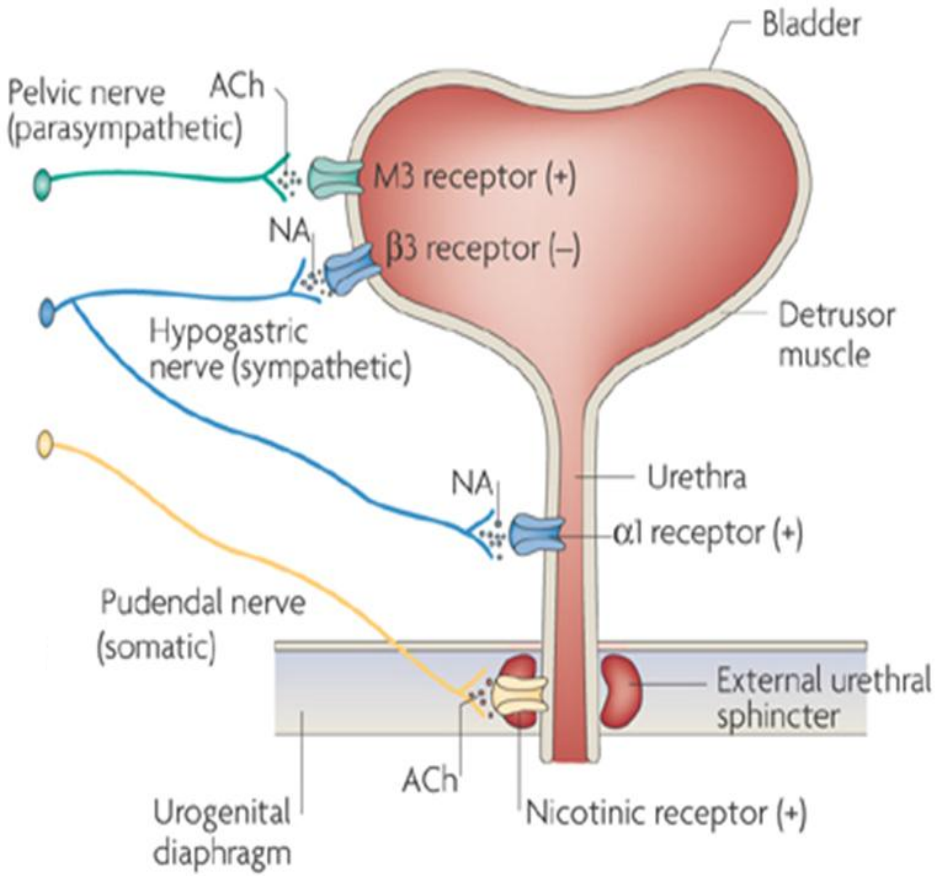
- The neural control of the lower urinary tract in health

- What happens following neurological injury

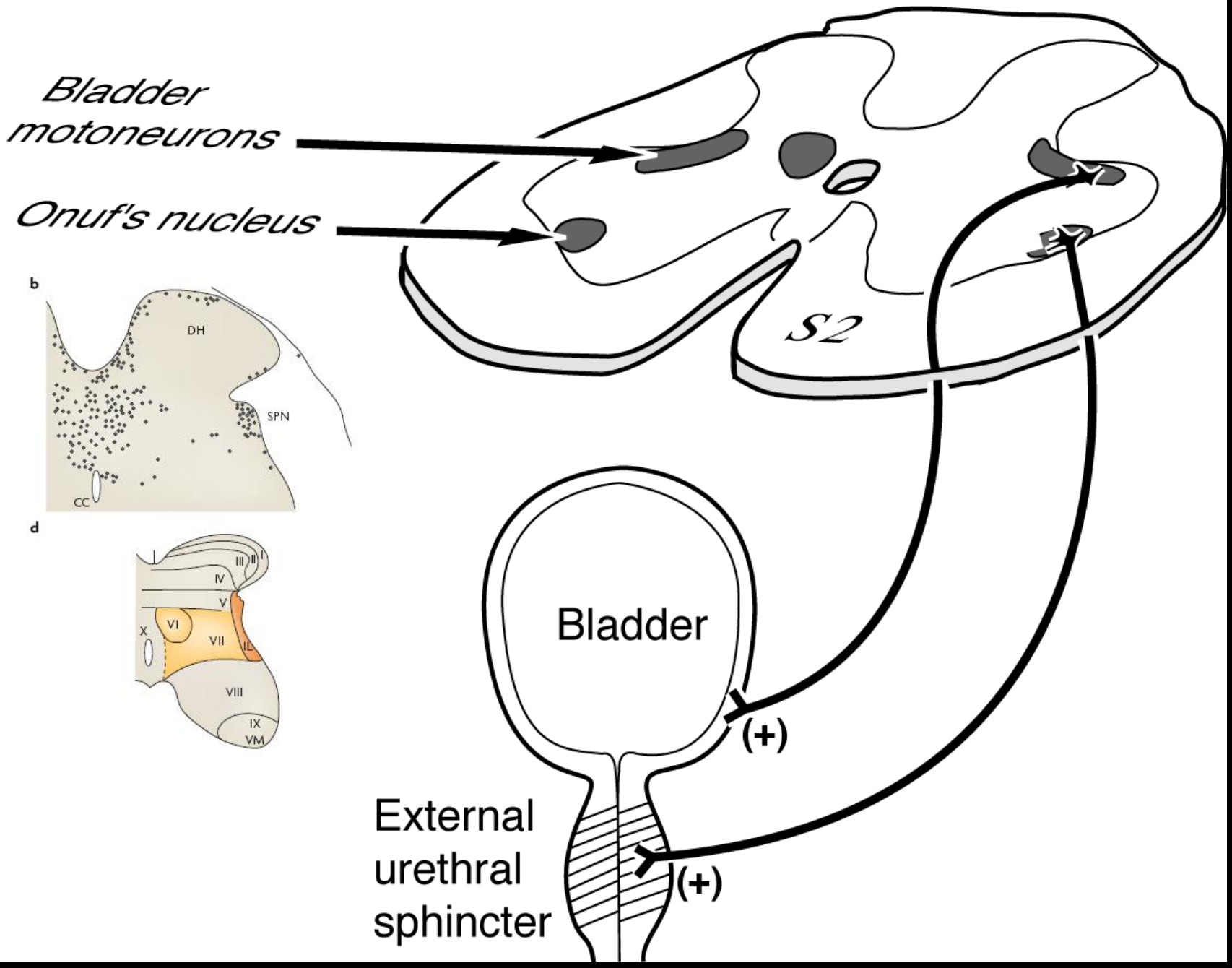
The neural control of the lower urinary tract..... is unique

- Dependence on the central nervous system
- Element of voluntary control
- Functions depend upon learned behaviour
- Neural circuitry: phasic vs tonic activity





Fowler, Griffiths, de Groat Nat Rev Neurosc 2008


Bladder motoneurons
Onuf's nucleus
b
DH
SPN
CC
d
I
II
III
IV
V
VI
VII
VIII
IX
X
IL
VM
S2
Bladder
(+)
(+)
External urethral sphincter

Spinal control

Storage

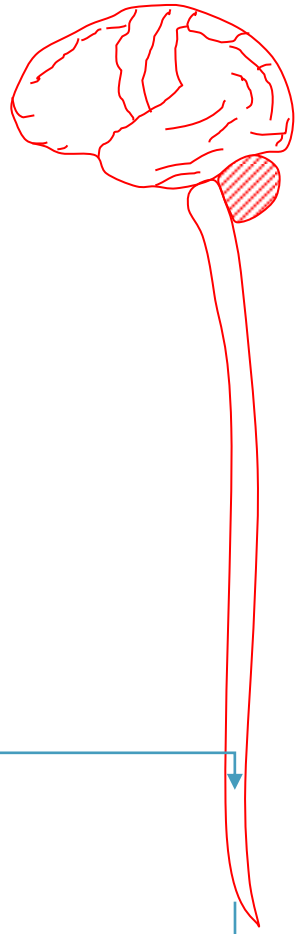
- *Bladder-to-urethra* procontinence guarding reflex
- Sympathetic mediated detrusor relaxation

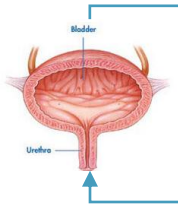
Full bladder

- *Bladder-to-urethra* inhibitory reflex
- *Bladder-to-bladder* excitatory reflex
- These form part of the spinobulbospinal reflex which allows higher centres to exert control over voiding

Emergence of central reflexes controlling LUT functions

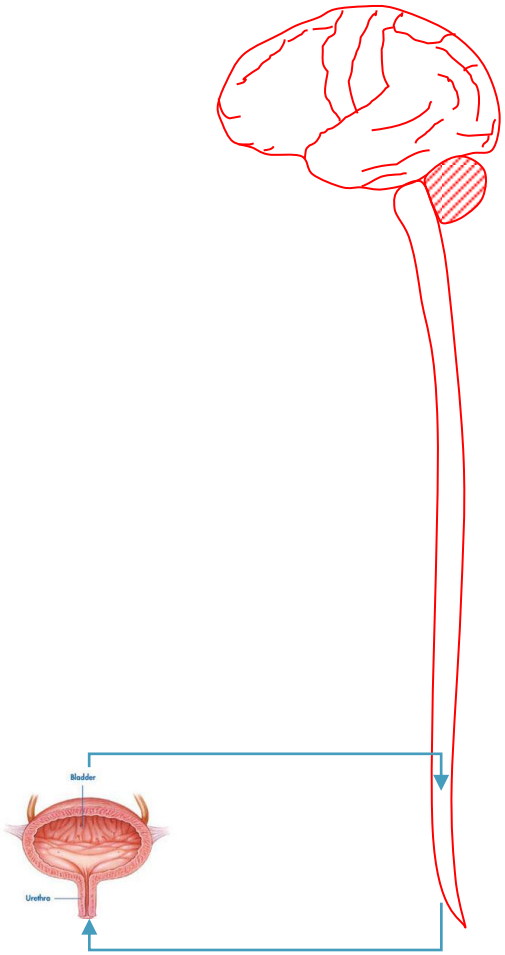
Cortical





Sacral spinal cord

Hierarchical control of LUT functions



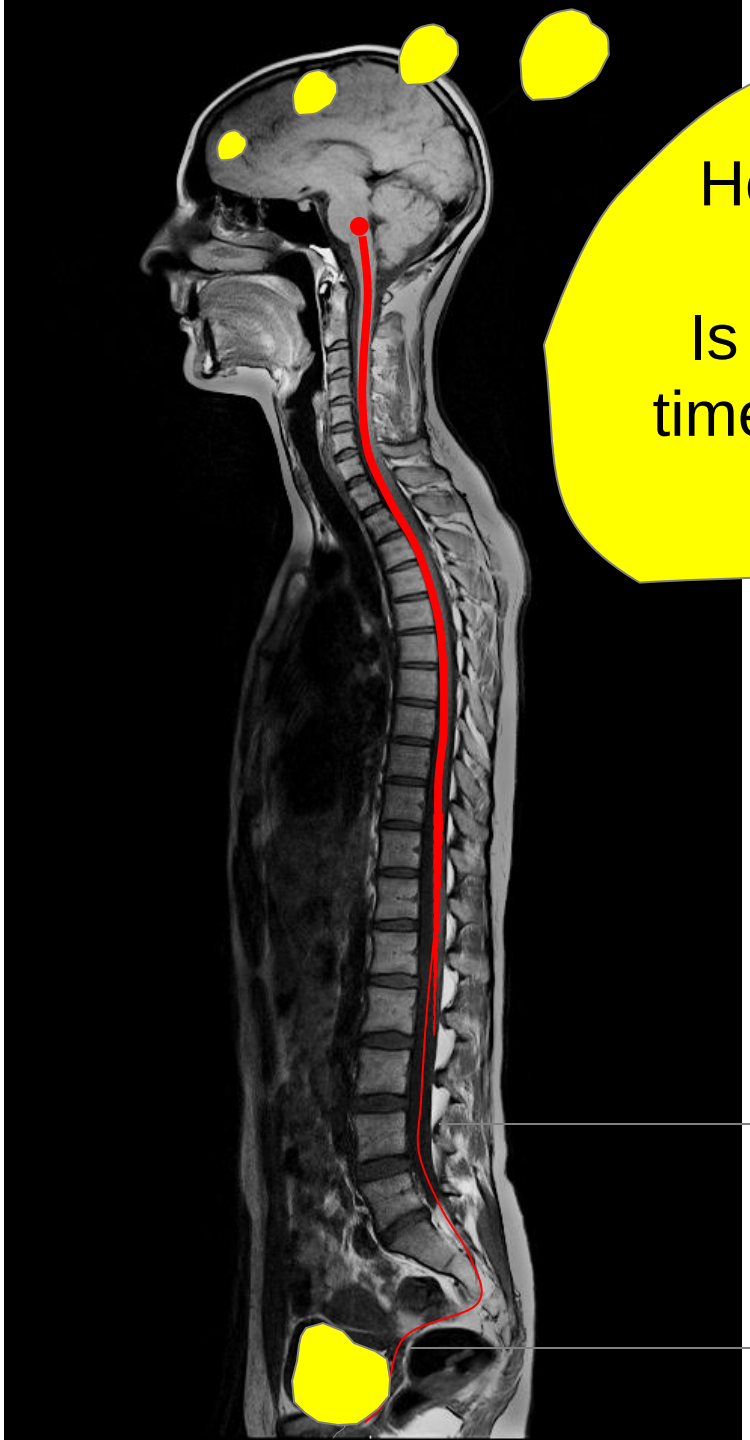
Cerebral cortex- sensations/
timing of micturition

Brain stem- coordination of reflexes

Spinal cord- amplification

Peripheral nerves- relay

Adapted from de Groat

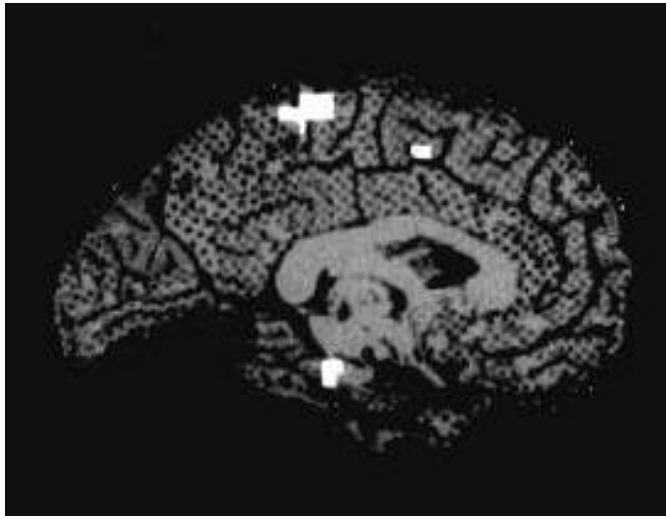


How full is my bladder?
Is this the right time and place to void?

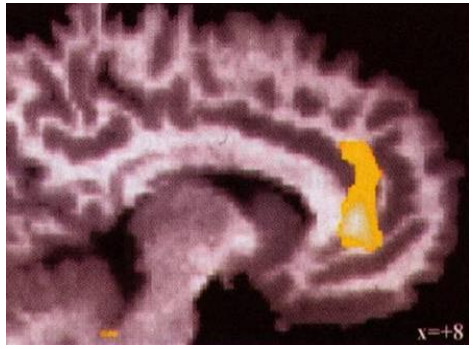
S2-4 in cauda equina

pelvic & pudendal ns

Functional brain imaging



SPECT
Fukuyama et al. *Neuroreport* 1996

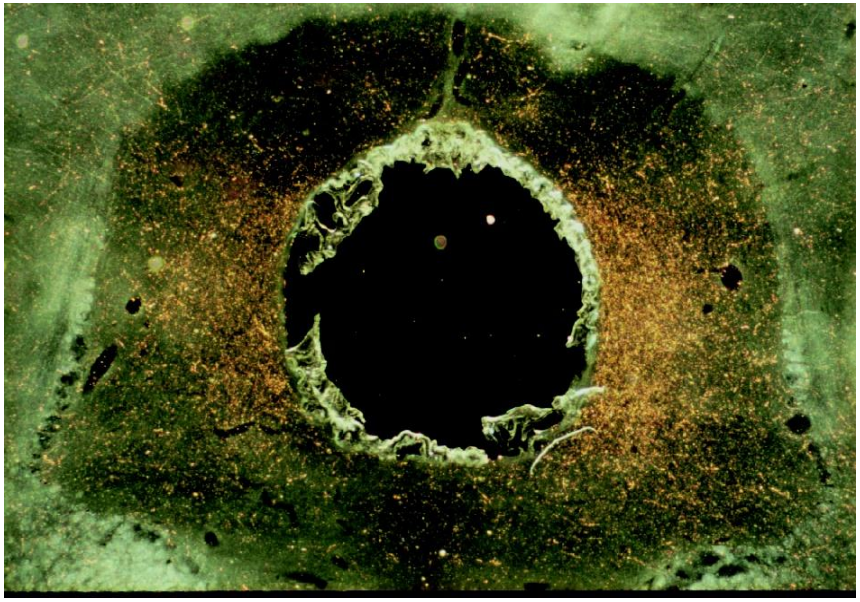


PET
Healthy males,
Blok et al. *Brain* 1997

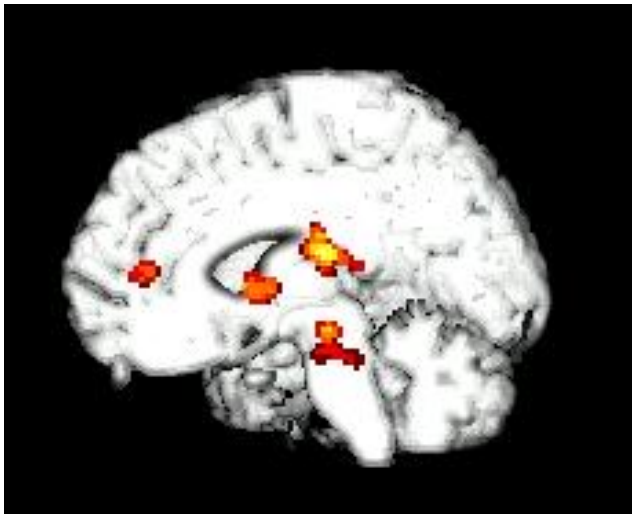
•Various paradigms used- repeated PFM contractions on full and empty bladder, alternating bladder filling and emptying

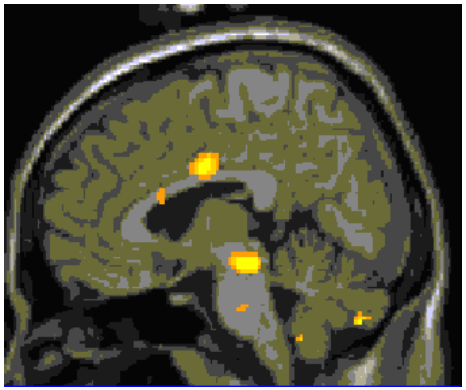
•Changes in cortical and subcortical activity during the micturition cycle

Perception of bladder fullness



Periaqueductal grey (PAG) of the midbrain
(courtesy Holstege)





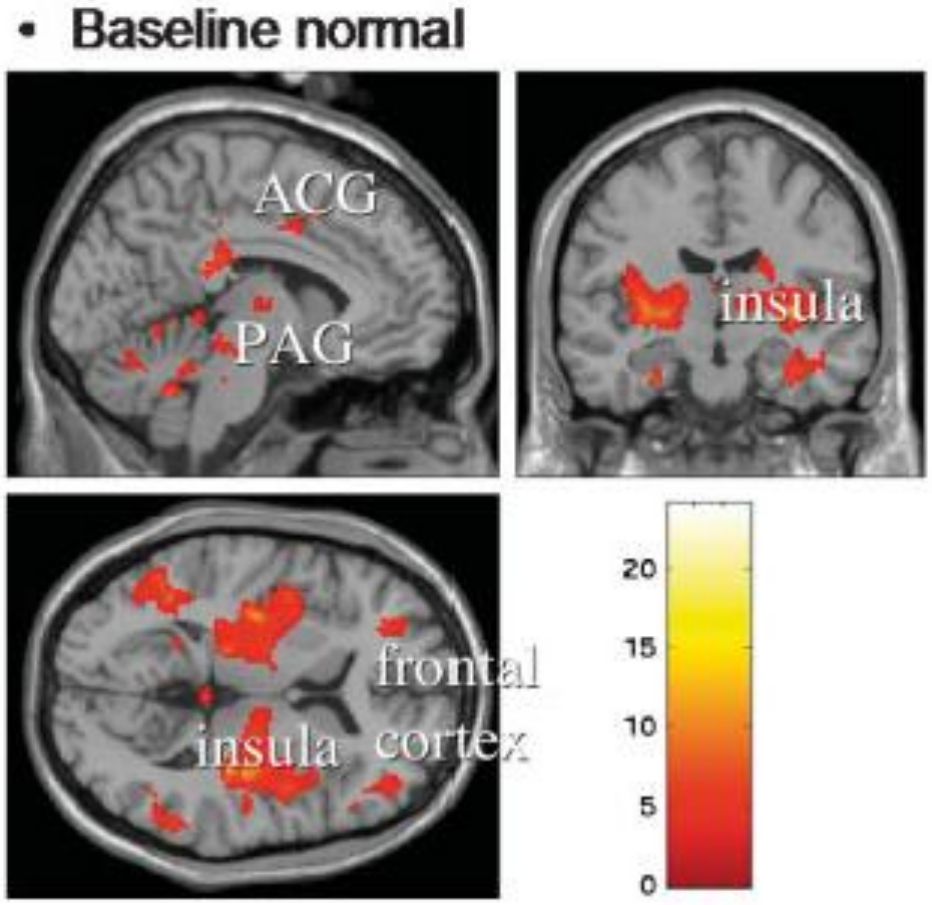
Matsuura et al, 2002
Athwal et al, 2001

Changes in brain activity with bladder filling- healthy controls

- Good bladder control

- Small volume infused
- Mild sensations

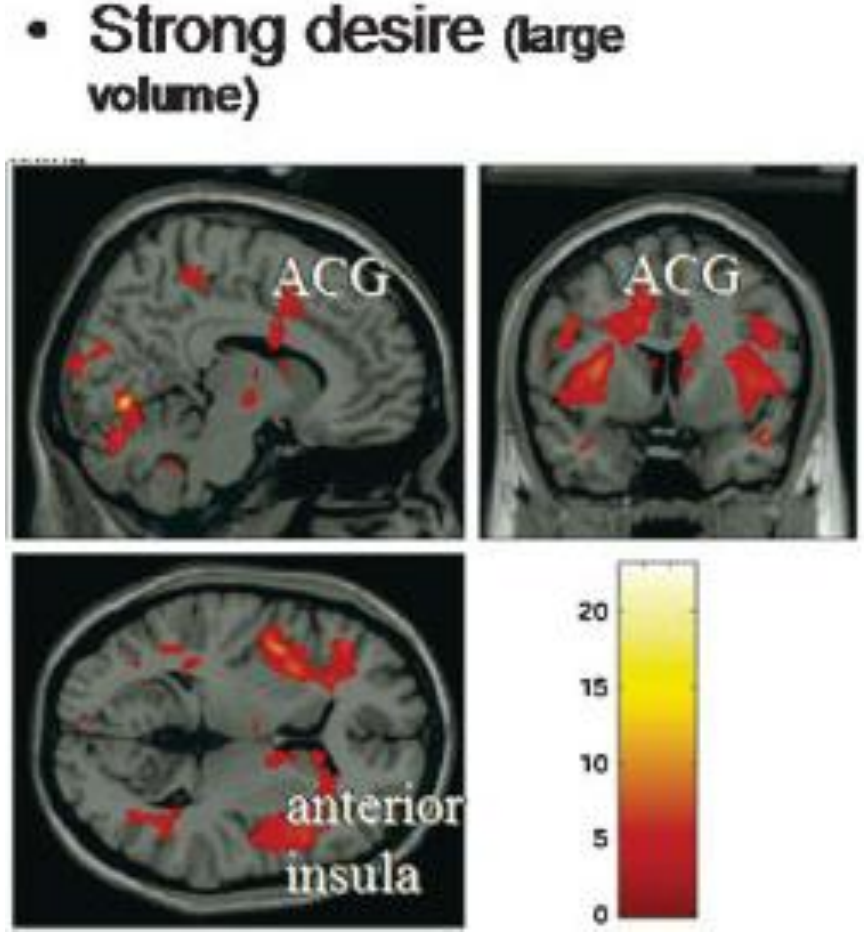
(n=6)



Griffiths D, Neurourol. Urodynam. 26:899–903, 2007

Changes in brain activity with bladder filling- healthy controls

- Good bladder control
- Large bladder volume
- Strong desire to void



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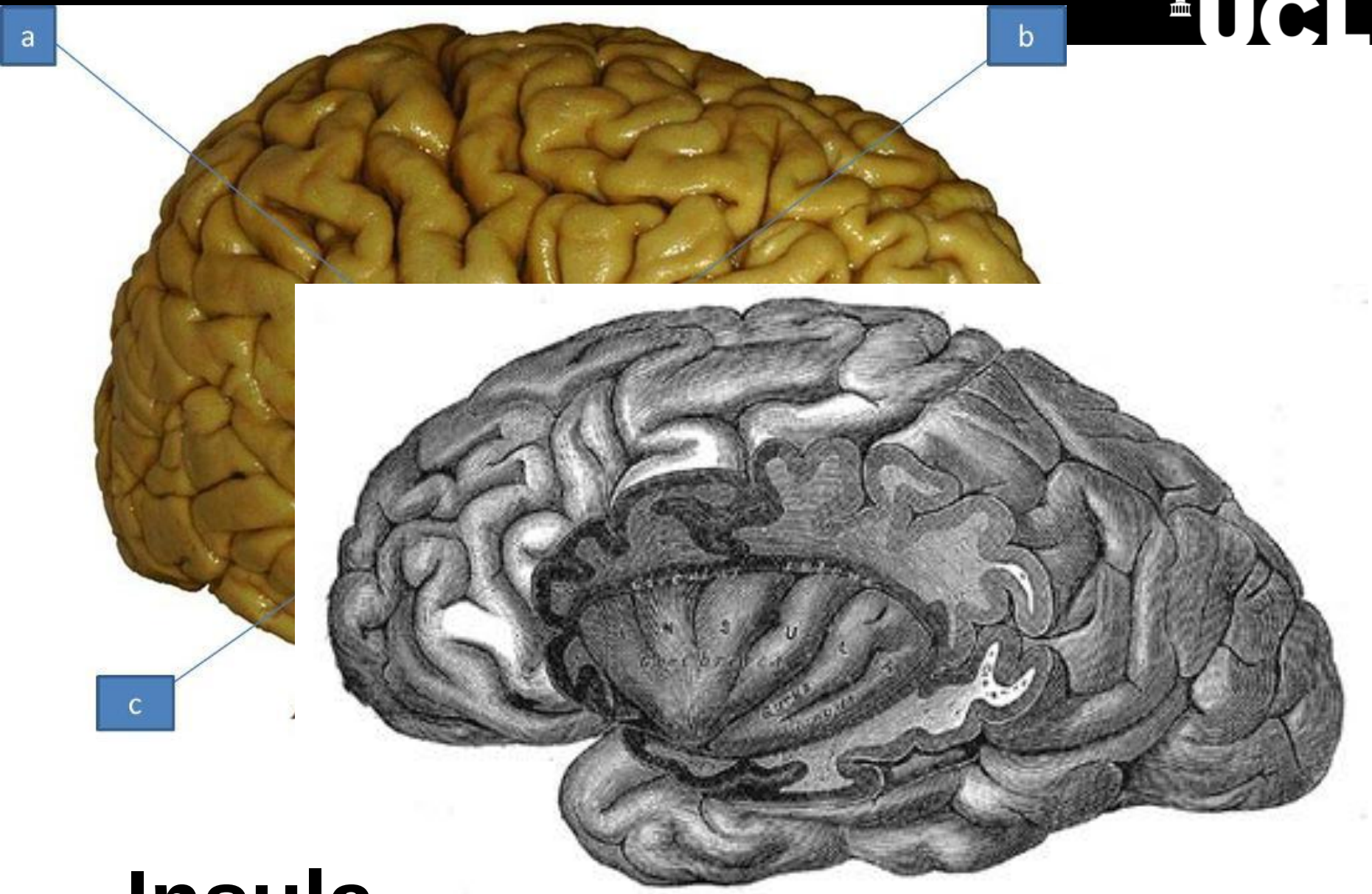
Griffiths D, Neurourol. Urodynam. 26:899–903, 2007



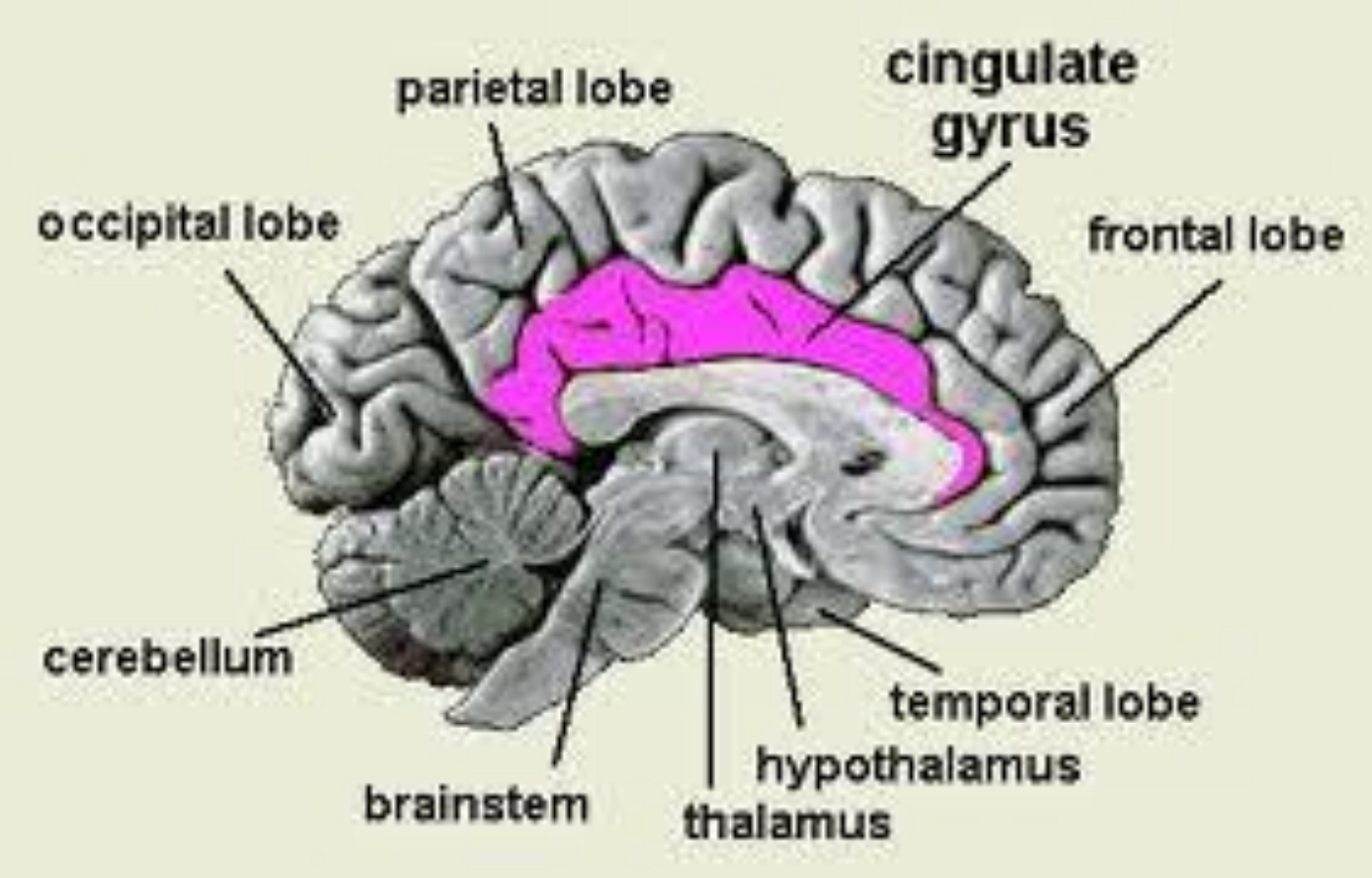
Insula

Gray's anatomy 1918

Insula = interoceptive or homeostatic afferent cortex

- The homeostatic afferents are the “missing” sensory limb of efferent autonomic nervous system
- Interoceptive sensations are associated with an affective, motivational aspect, hence their value in homeostasis.
- Afferents from PAG are mapped in the insula
- Basis of bladder sensations

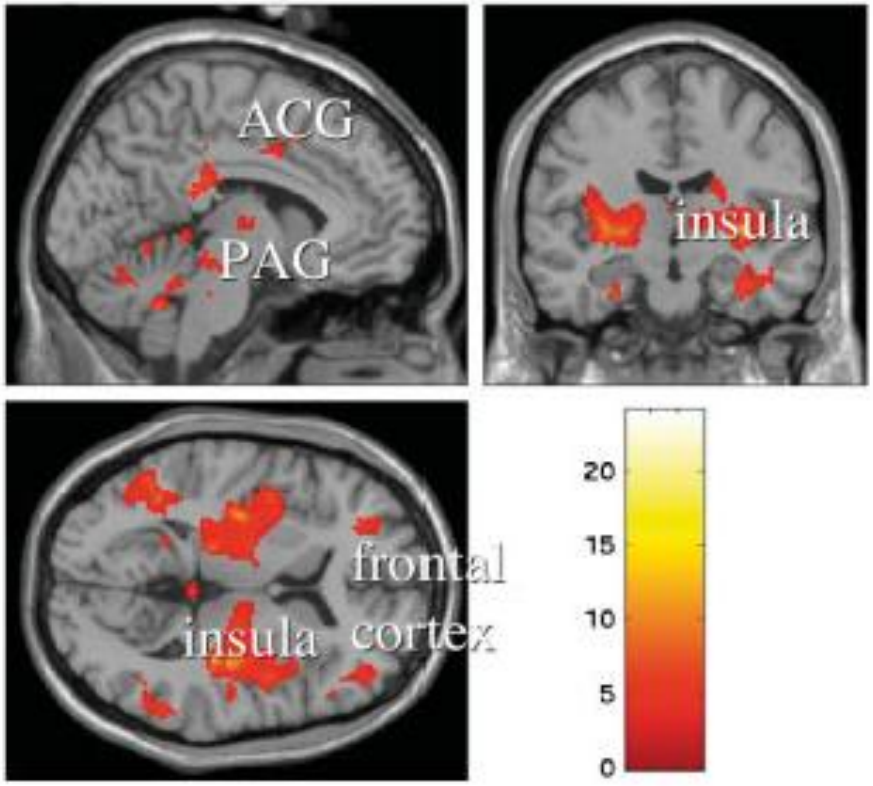
Cingulate cortex



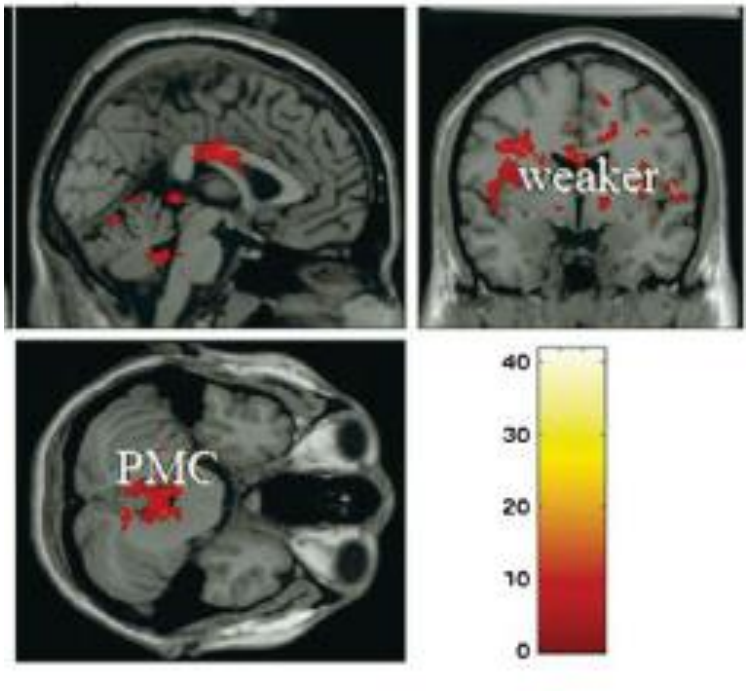
- ACC associated with motivation and affective aspect of interoceptive sensations
- Output correlates with sympathetic activation
- Insula= “limbic sensory cortex”
- Anterior Cingulate Cortex = “limbic motor cortex”
- Both frequently co-activated
- Monitoring and control as bladder is filling
- Inhibits voiding through the PAG
- With filling, activation shifts anteriorly- associated with “unpleasantness”

Changes in brain activity with bladder filling- patients with poor bladder control

- Baseline normal



- Poor control
- Small bladder volume

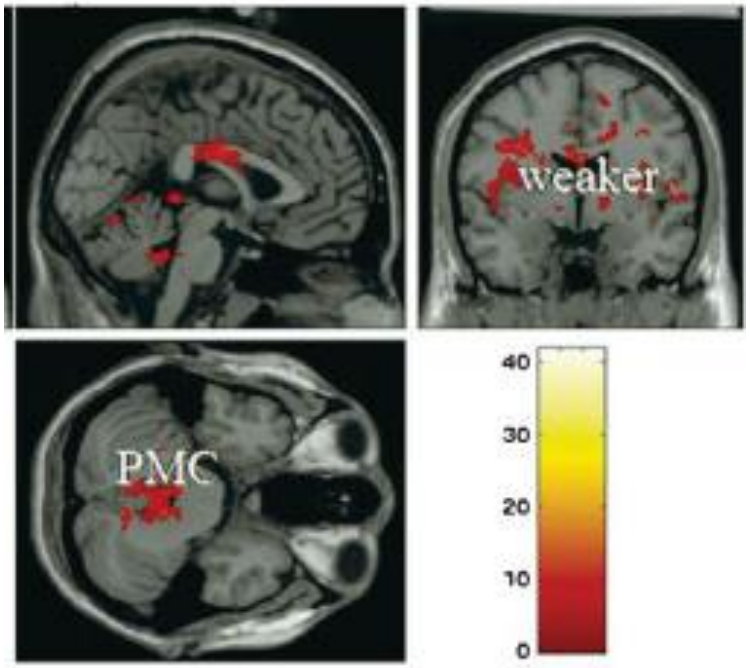


(n=5)

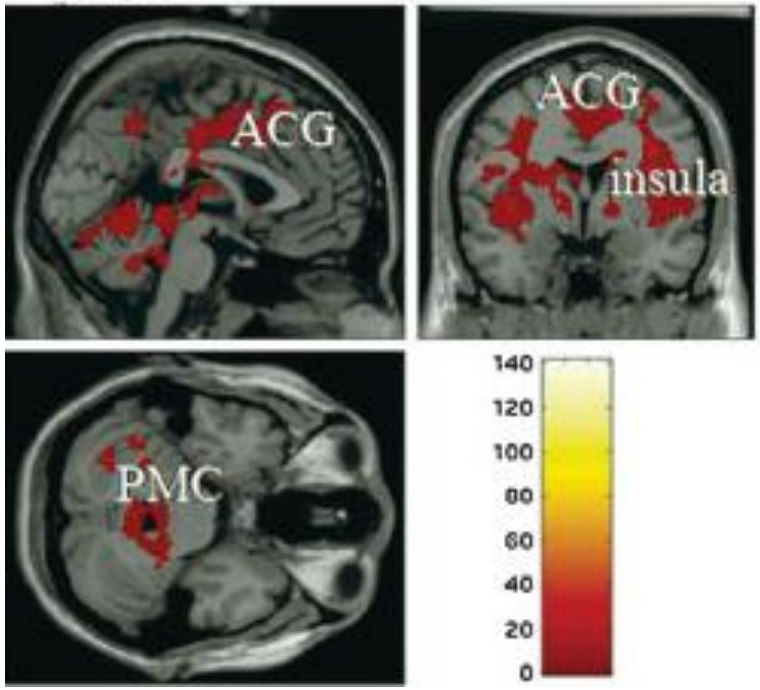
Griffiths D, Neurourol. Urodynam. 26:899–903, 2007

Changes in brain activity with bladder filling- patients with poor bladder control

- Poor control
- Small bladder volume



- Poor control, strong desire to void, no actual DO

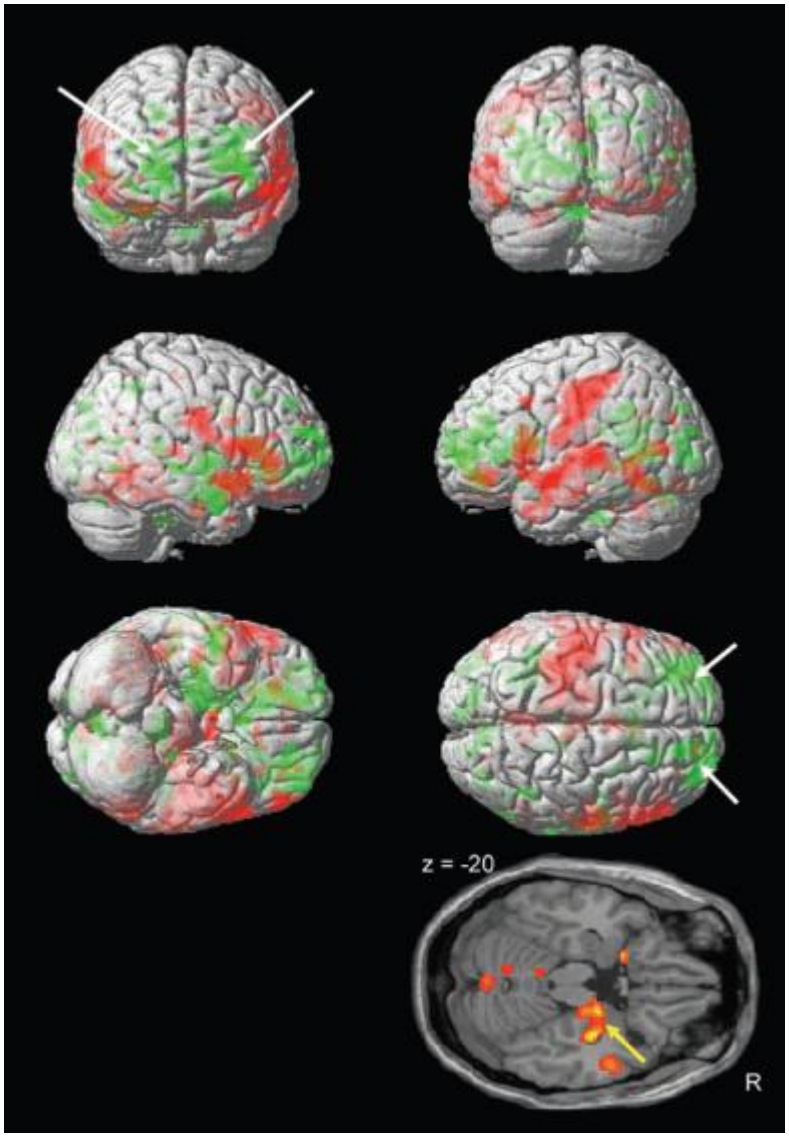


(n=5)

Griffiths D, Neurourol. Urodynam. 26:899–903, 2007

Changes in brain activity with bladder filling- DO during scanning

- Women with urinary urgency
- DO in the scanner

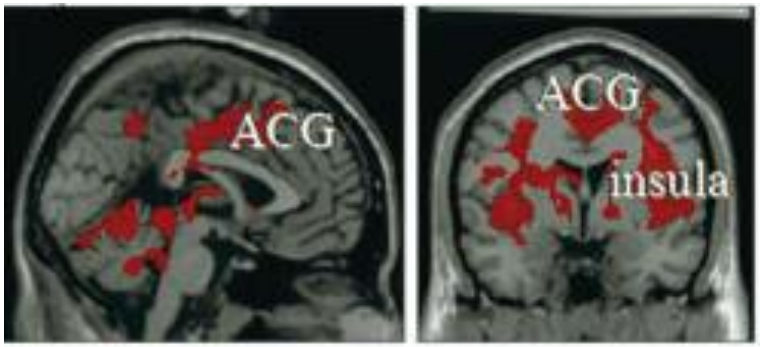


N=3

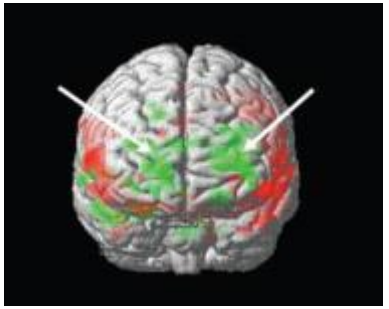
Griffiths and Tadic. Neurourol. Urodynam. 27:466–474, 2008

Patterns of brain activity in patients with poor bladder control

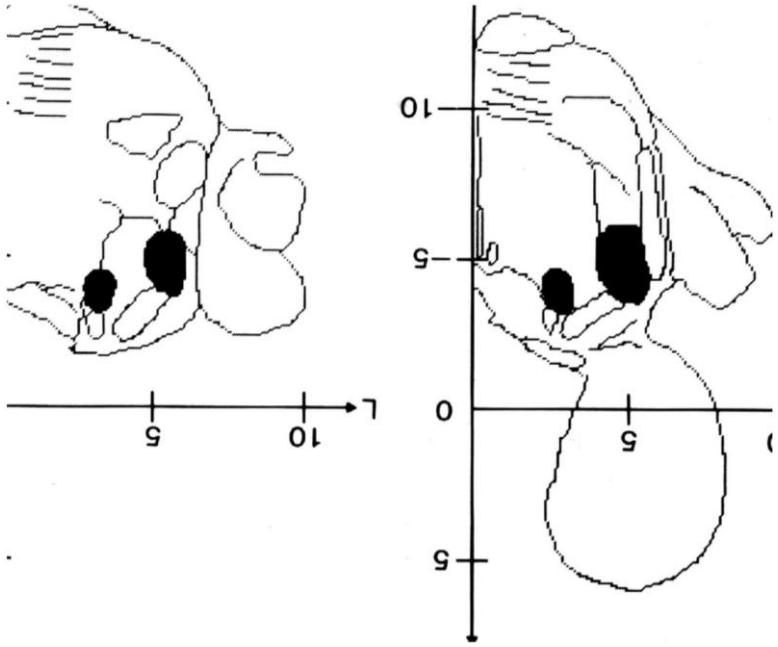
Anterior cingulate- urgency



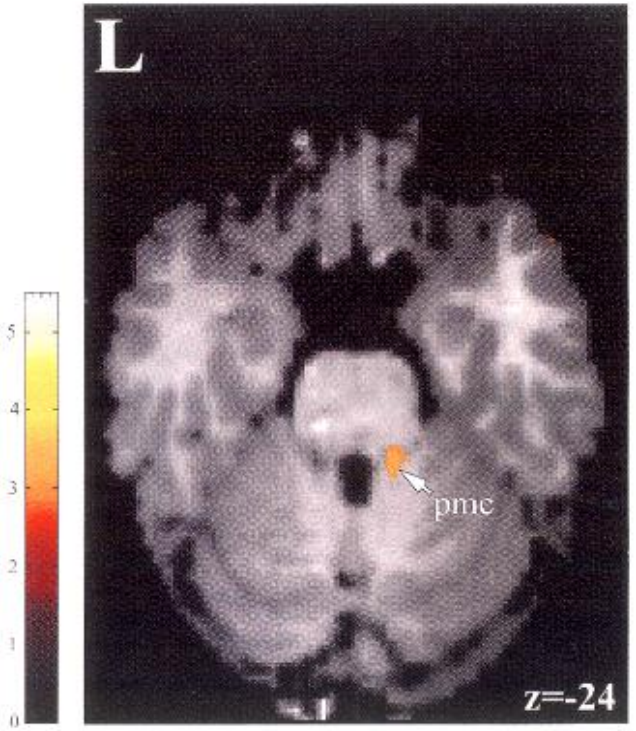
Prefrontal cortex- continence mechanism



Pontine micturition centre = “Barrington’s nucleus”

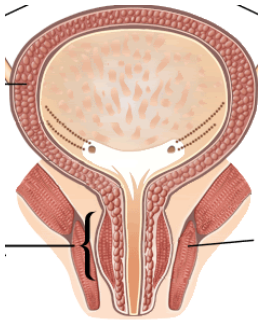


Griffiths, Holstege et al., 1990 in cat



Blok et al, 1997

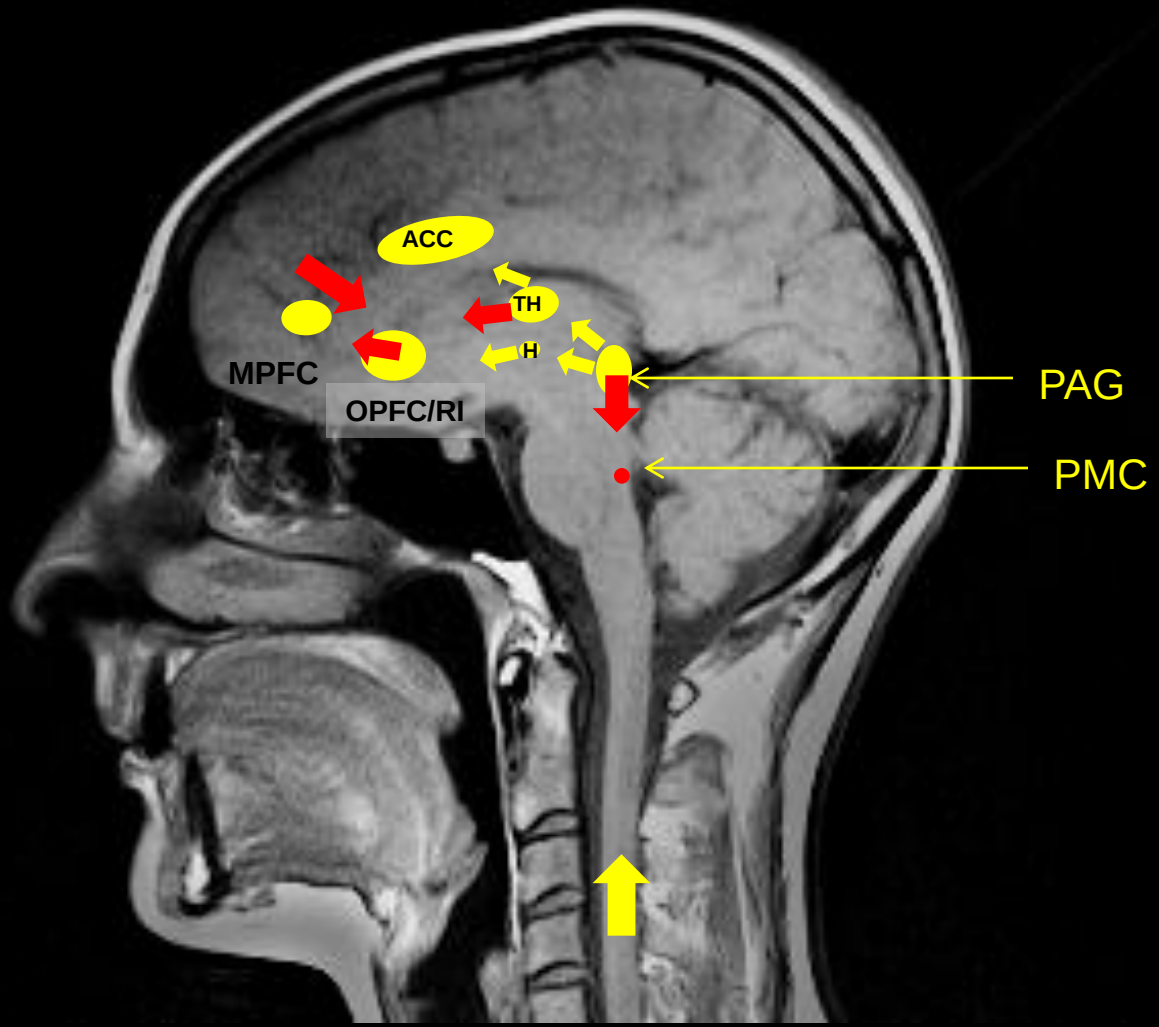
LUT control: two neural programs and a switch



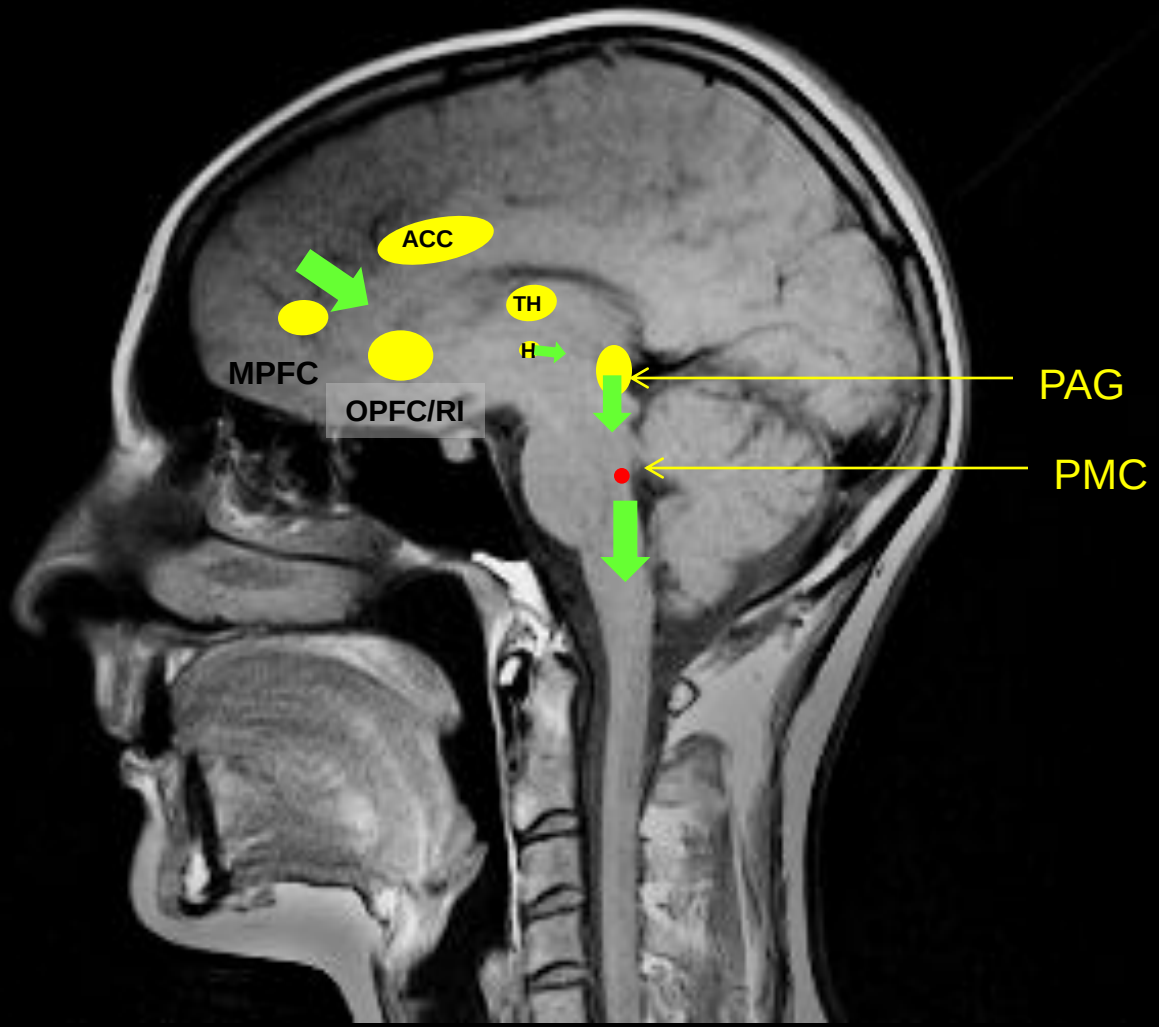
> 99%

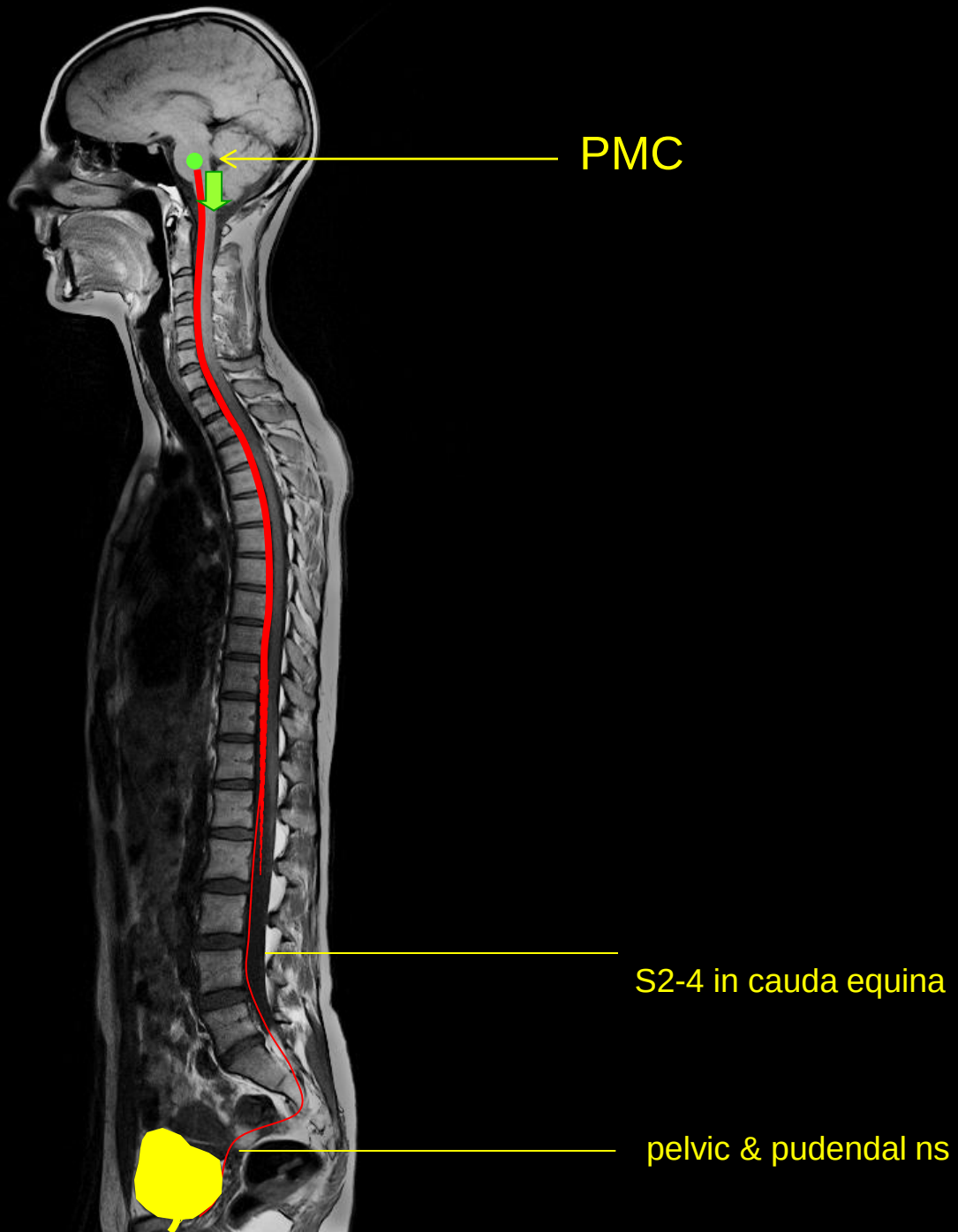
Detrusor	Sphincter
Storage phase	**Relaxed**	**Active**
Voiding phase	**Active**	**Relaxed**

Storage



Voiding




PMC
S2-4 in cauda equina
pelvic & pudendal ns

Suprapontine

Stroke
Parkinson's Disease
Tumours
Trauma
Dementias

Spinal

Multiple Sclerosis
Trauma
Tumour

Sacral / Infrasacral

Disc prolapse
Tumour
Pelvic nerve injury
Small fibre neuropathy

- Storage symptoms
- PVR: < 100mL
- Detrusor overactivity

- Storage / voiding symptoms
- PVR: usually elevated
- Detrusor overactivity, detrusor sphincter dyssynergia

- Predominantly voiding symptoms
- PVR: elevated
- Often acontractile detrusor