

COMORBIDITY BETWEEN ENURESIS NOCTURNA, HYPERACTIVITY AND SLEEPDISORDERS

J.Vande Walle, K.Dhondt, C. Van Herzeele, A.Raes,

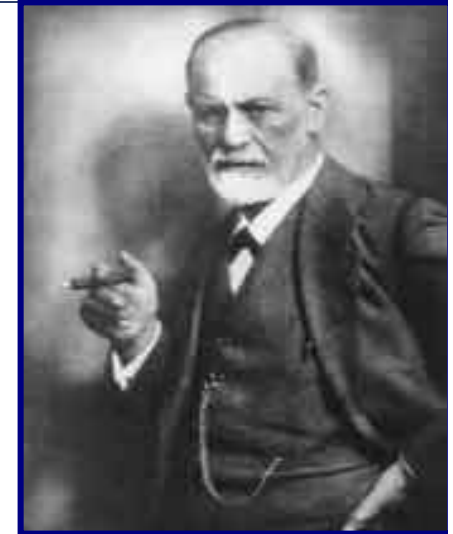
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NEUROLOGIE

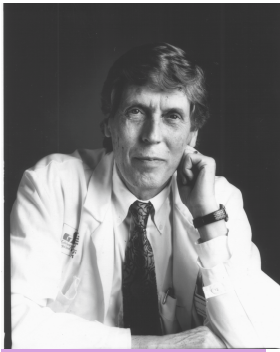
Nocturnal enuresis



Introduction Before 1989

- **Nocturnal enuresis**
 - Was a benign condition
 - Not harming anybody
 - Selflimiting.. since it disappeared spontaneously
 - Not necessary to treat, except in rare cases
 - And if there was a cause..it was generally accepted that it had to be a psychological cause





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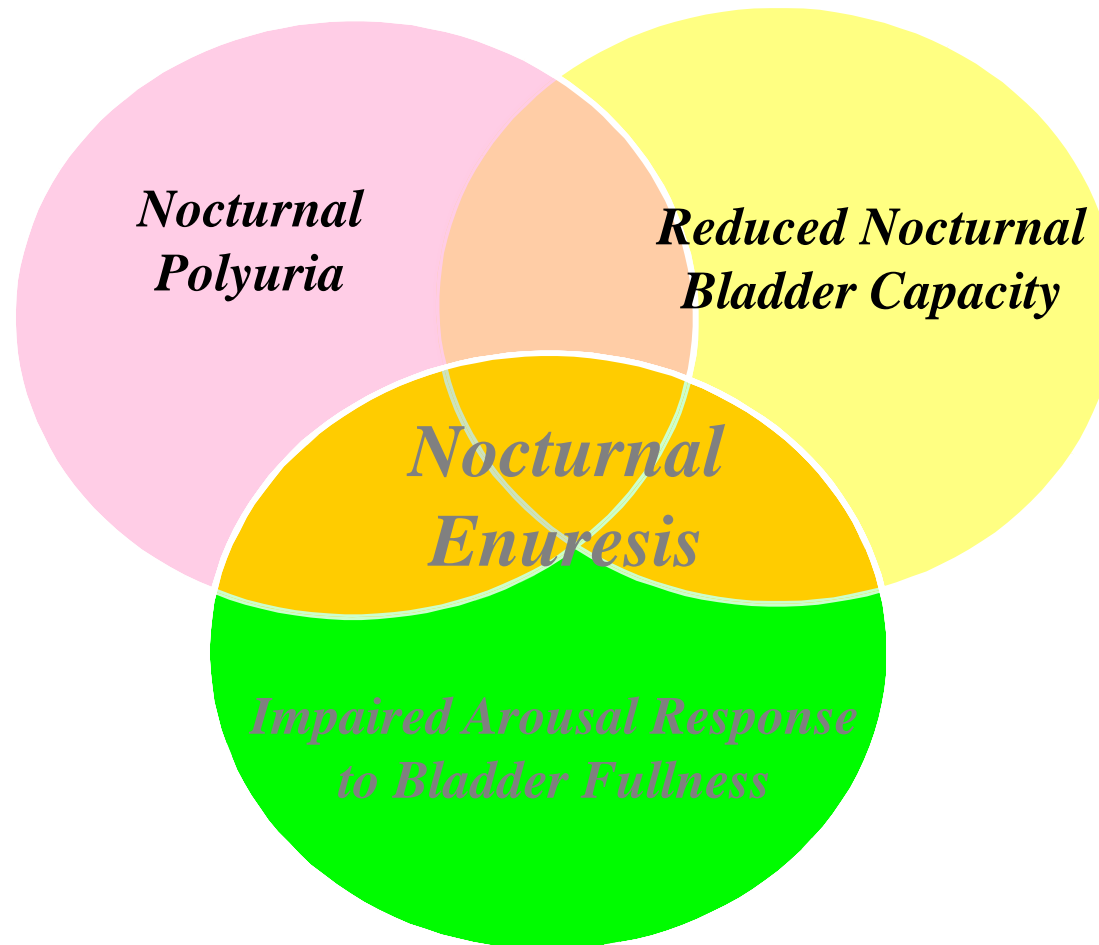


Introduction 1989-2009

- **enuresis is an organic condition**
 - Caused by hereditary factors
 - Subdivided into Non monosymptomatic / monosymptomatic enuresis
- **Where MNE is characterised by**
 - A mismatch between nocturnal diuresis volume and functional bladder volume
 - Only spontaneously disappearing in mild cases, without comorbidity factors



Pathophysiology of Nocturnal Enuresis



(A heterogeneous disorder)

Percentile 2011

- ➔ **Back to history**
- ➔ **Forget the whole article**

Introduction 2009 - 2019

- **enuresis is an organic disease**
 - A mismatch between diuresis volume and functional bladder volume overnight / hereditary (genes)
 - “Only” spontaneously disappearing in mild cases
 - Importance of **comorbidity** factors
 - With **severe** psychological consequences
 - For child (selfesteem, burden), and and family (intolerance)
 - **With significant influence on cognitive functions of the child**
 - **making a wait and see attitude is not longer defendable**



man, vrouw en kind

Universitair Ziekenhuis Gent



Cognitive disturbances following night-time wetting in children

1. **The CK Yeung theory**
2. Is there evidence ?

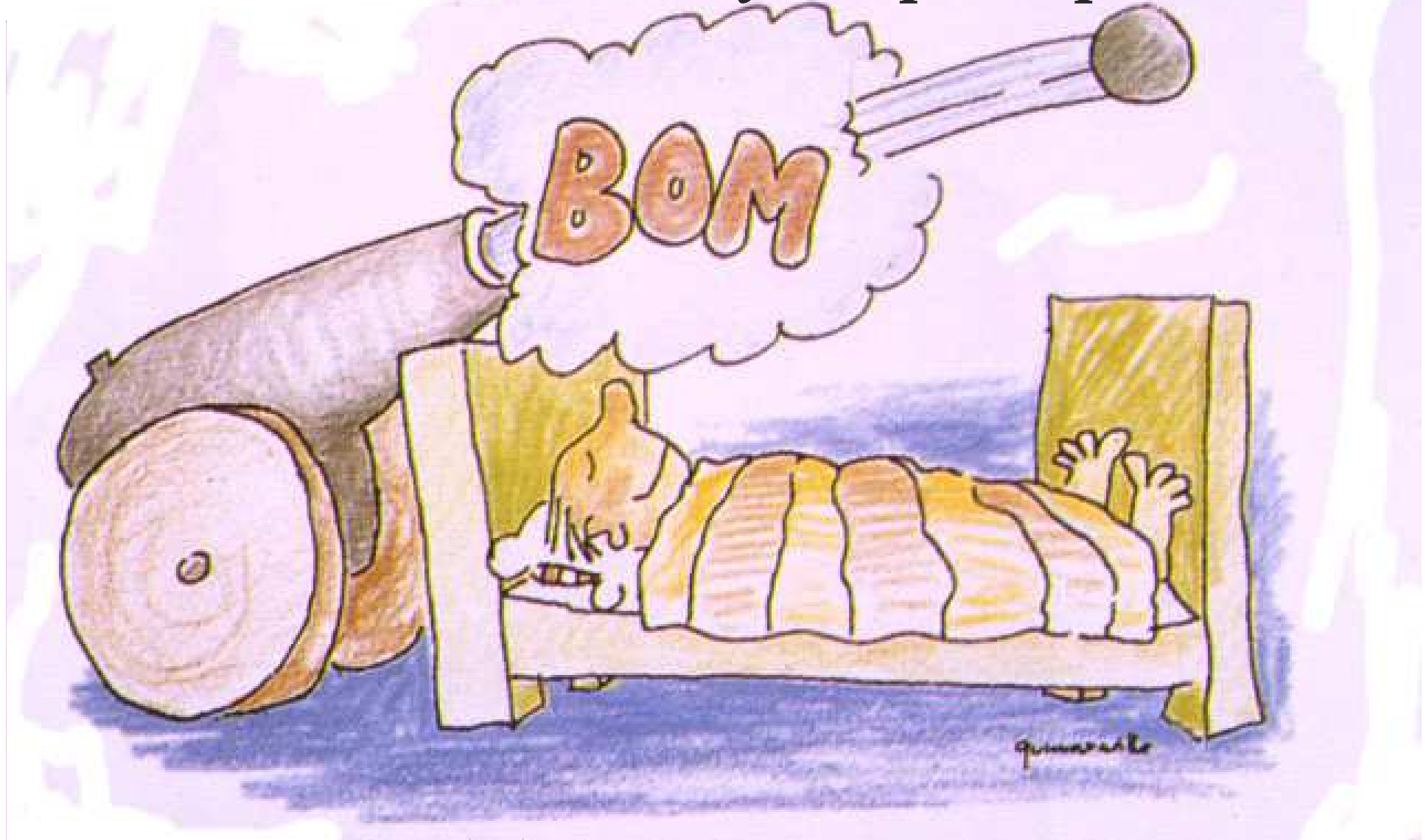


CK Yeung ICCS Hong Kong 2006

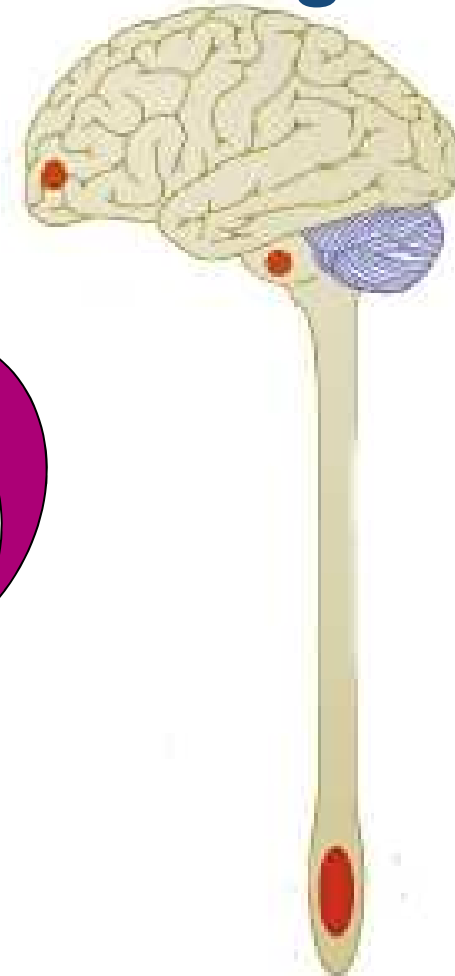
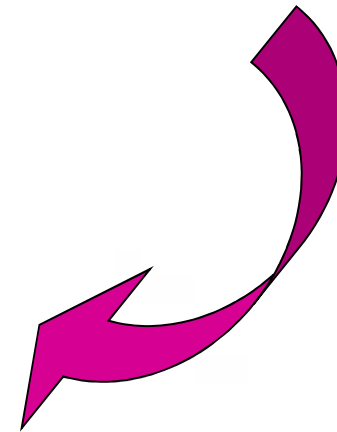
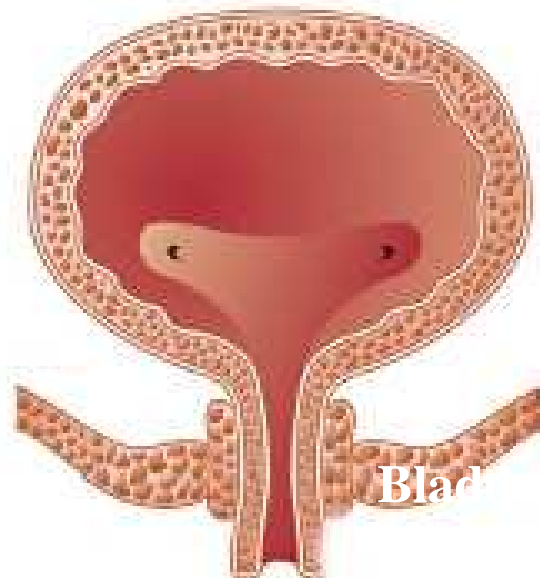
Correlation between

1. Enuresis
2. Bladderdysfunction
3. Attention deficit
4. Sleep disturbances

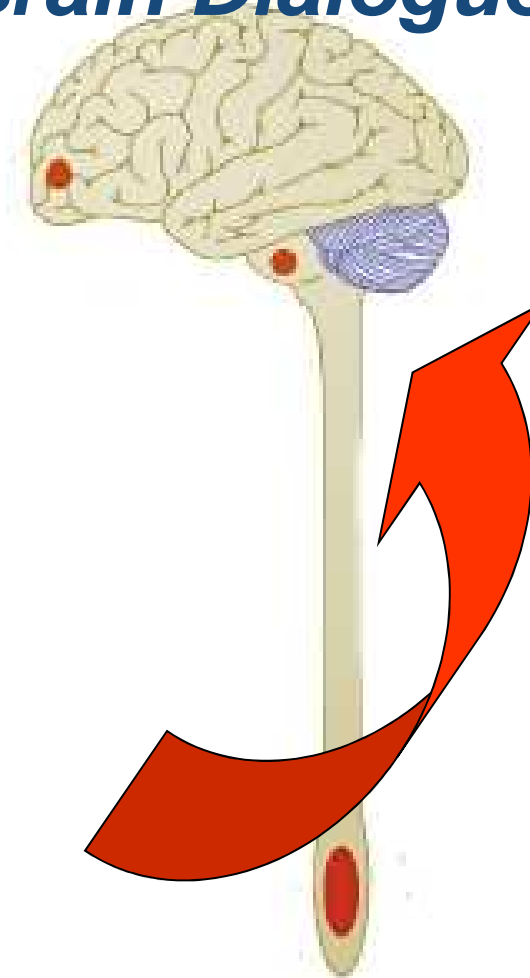
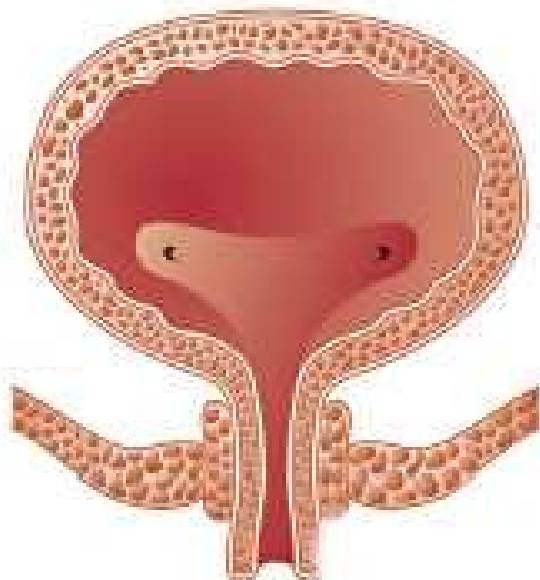
Are Enuretics Really Deep Sleepers ??



Does a Bladder-and-Brain Dialogue exist??



Does a Bladder-and-Brain Dialogue exist??





CK Yeung ICCS Hong Kong 2006

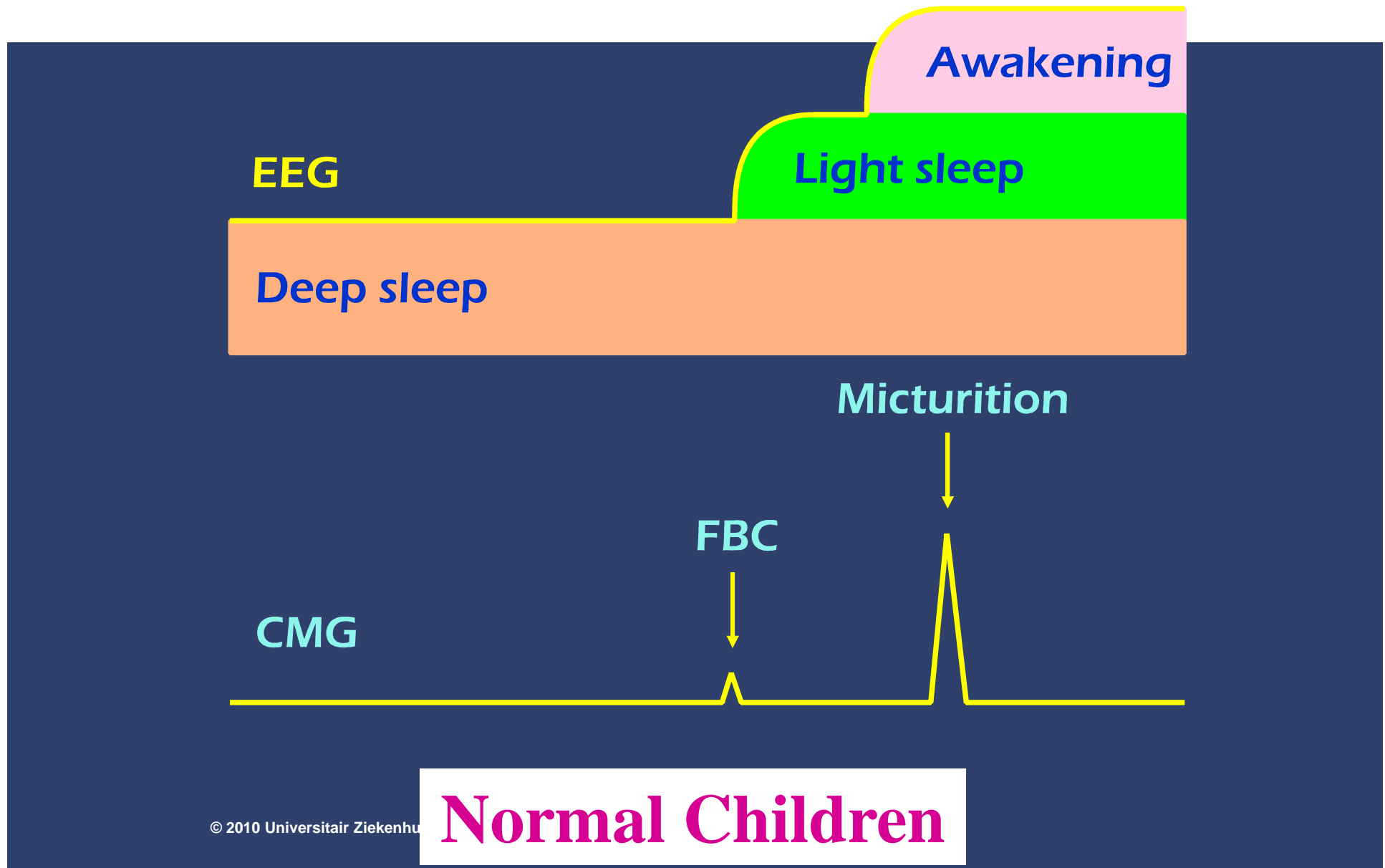
1. **Bladder function tests**
2. **Sleep Architecture and Cortical Arousal**
3. **Brainstem Function**
 - ➔ Prepulse Inhibition of Startle (PPI) Reflex
 - ➔ Latency P300 event-related brain potential (ERP)
4. **Cognitive Performance-tests**
 - ➔ intelligence score (Raven Progressive Matrices Test)
 - ➔ focused attention (Digit Cancellation Test)
 - ➔ short-term memory (HK List Learning Test)
 - ➔ retention ability & long-term memory (HK List Learning Test)
 - ➔ shifted attention, learning speed and reaction (Conner's Continuous Performance Test)

In patients with enuresis worse than in controls

But normalises after therapy

But data remain unpublished

Bladder Behaviour and Sleep Changes



Normal Children

Bladder Behaviour and Sleep Changes

EEG

Light sleep

Deep sleep

Micturition

CMG



Enuretic Children





HANGOVER THE OVER



WHAT HAPPENED LAST NIGHT?

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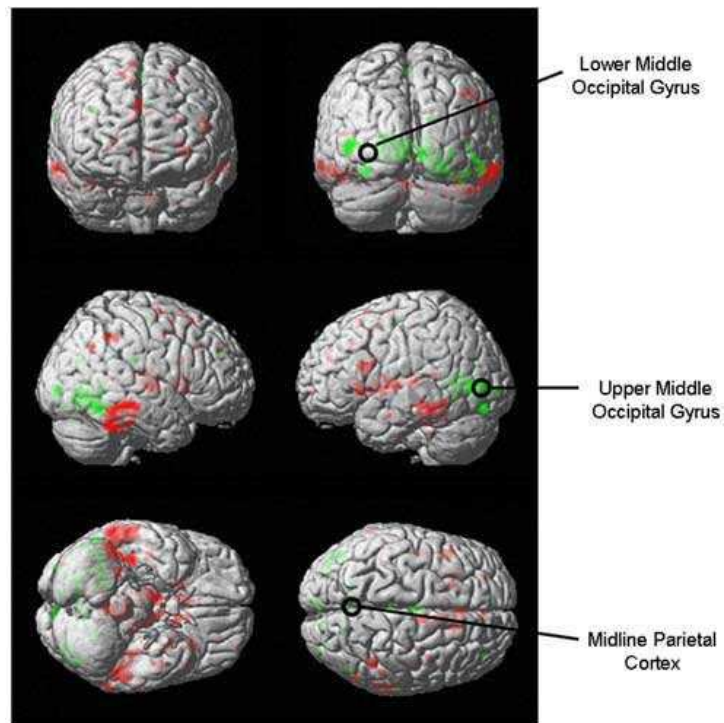
Theory from CK Yeung

- **Nocturnal enuresis**
 - Causes sleep disturbance
 - Overstimulation of central brain
 - Cognitive dysfunction
- **Treatment of nocturnal enuresis**
 - Amelioration of sleep
 - Less exhaustion of the brain
 - Amelioration of cognitive function

Animal model



Animal model cerebral dysfunction



Brain Region Affected by Sleep Deprivation Identified



Theory from CK Yeung

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CK Yeung ICCS Hong Kong 2006

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In patients with enuresis worse than in controls

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But data remain unpublished

Cognitive disturbances following night-time wetting in children

1. The CK Yeung theory
2. **Is there evidence ? NO = NO publication**

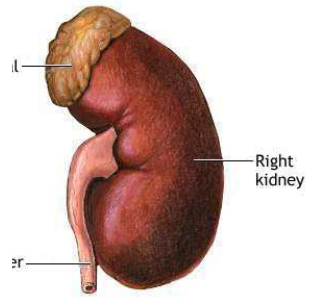
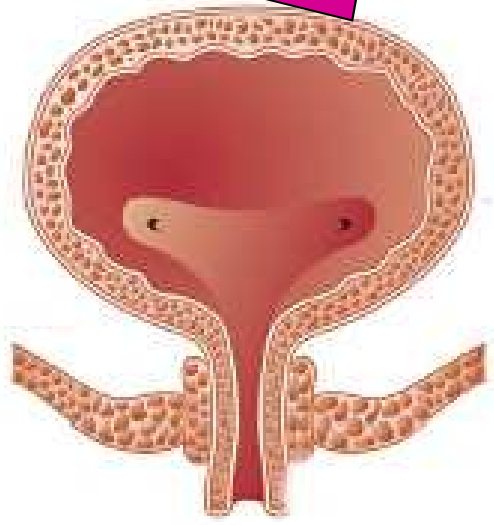
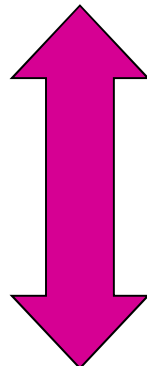
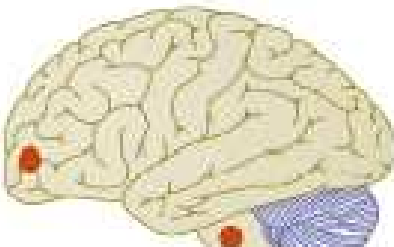
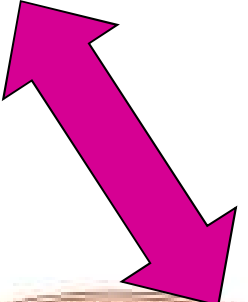
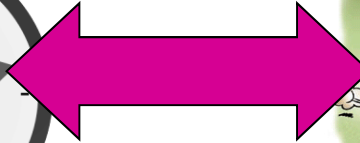
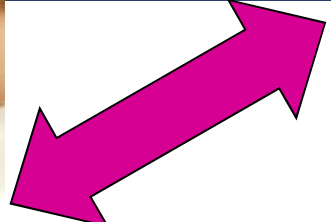
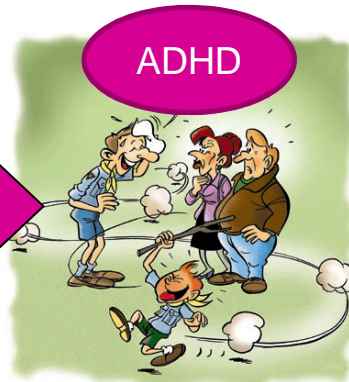
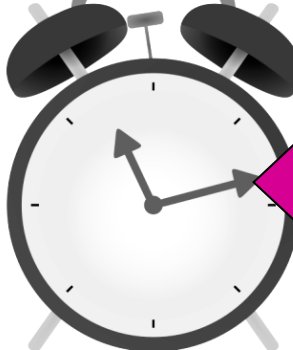
Is there evidence ?
Comorbidity = yes / causality = No/ = circulus viciosus

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Circadian rythm

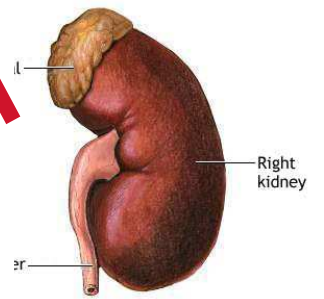
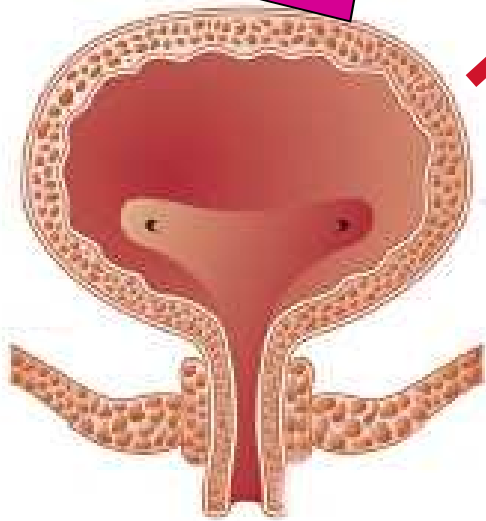
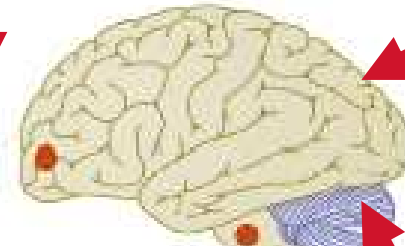
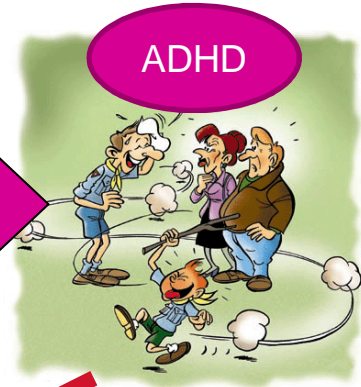


ADAM.

Circadian rhythm



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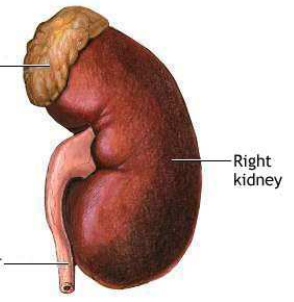
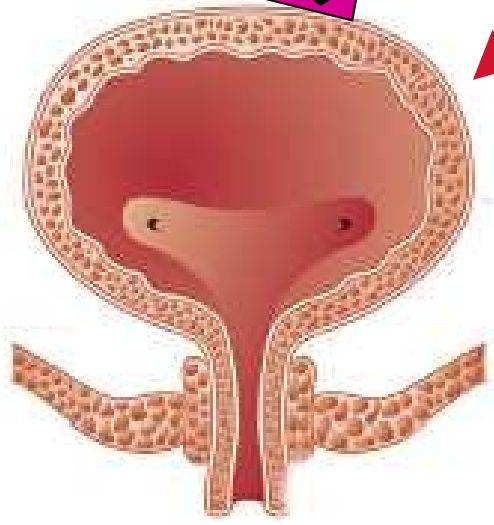
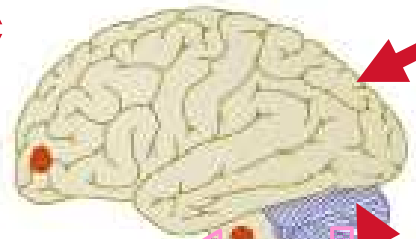
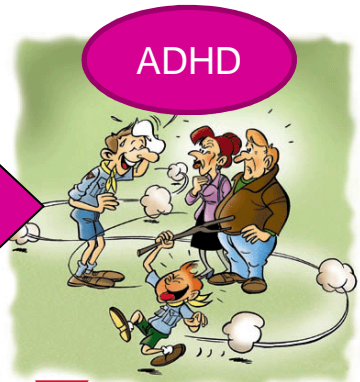


ADAM.

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Circadian rythm



Typ hier uw tekst

K. DHONT

S. RITTIG

C.K. YUING

D. BAEYENS

S. RITTIG

J. VANDE WALLE

ADAM.

The egg/ chicken

sleep



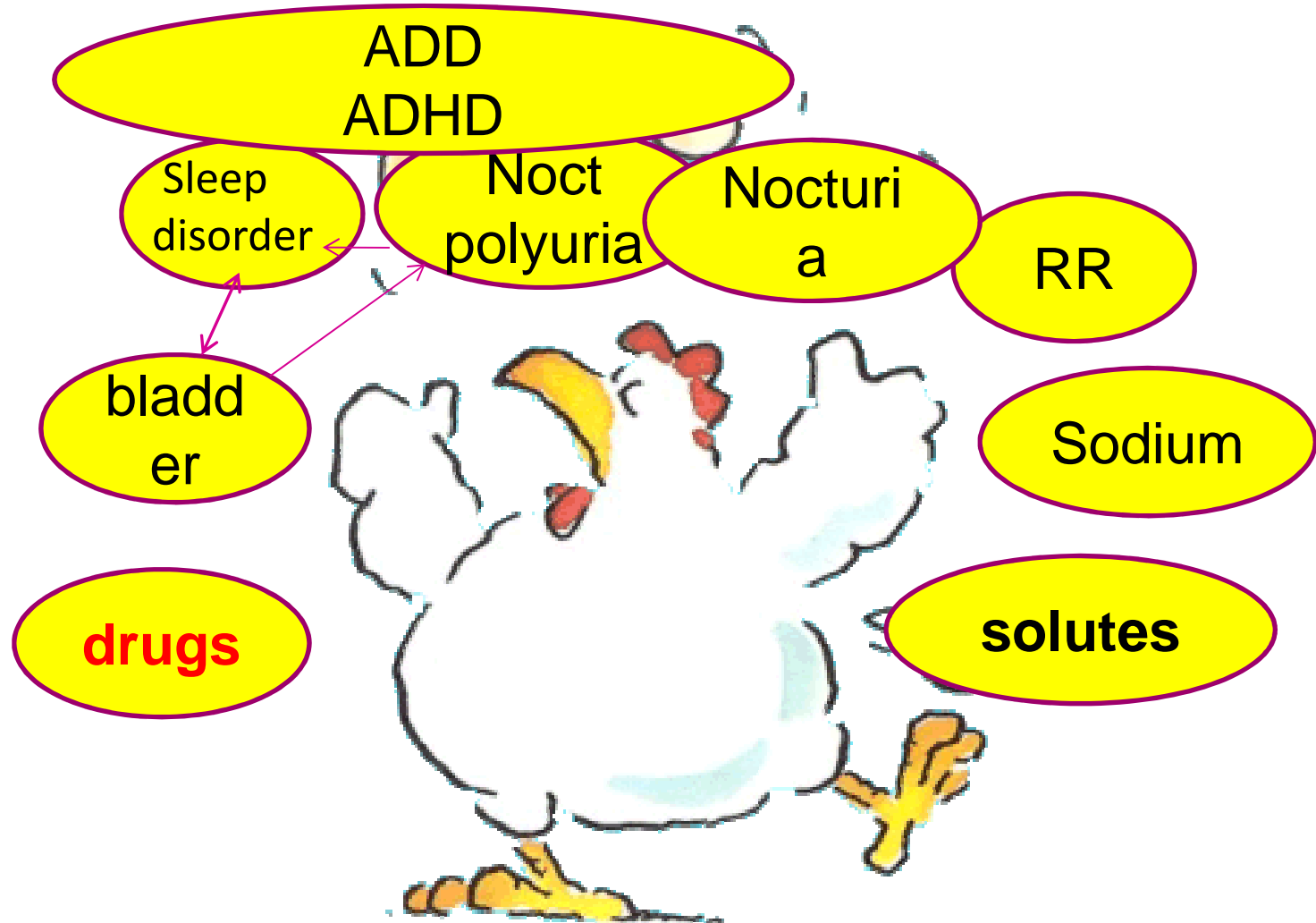
ADHD

Cognitive dysfunction

Therapy resistance

Diuresis/
Bladder

enuresis



OAB coincides with sleepdeprivation / ADHD symptoms (CK Yeung)

- **1999 Scan J U N Suppl**
**sleep disturbances and bladder dysfunction:
common in treatment-resistant enuresis**
- **2008 N Engl Med (letter)**
 - interaction between bladder overactivity and brain arousability
 - NE → more **lighter** sleep associated with
 - (1) frequent cortical arousals**
 - (2) inability to awaken completely**
 - Transition from light sleep to complete awakening may be suppressed by long-term overstimulation by signals from the bladder

OAB coincides with sleepdeprivation / ADHD symptoms (CK Yeung)

➤ 2009 Ped Urol Suppl (6 months treatment)

- sleep awakening threshold ↓
- number of awakenings ↑
- P300 ERPs latency ↓
- PPI of startle amplitude ↓

→ **brain function normalized in parallel to ↓ bladder dysfunction**

• 2010 J Urol (Xiang et al)

functional brainstem changes in response to bladder function alteration
elicited by surgical reduction in bladder capacity

Sleepdeprivation results in

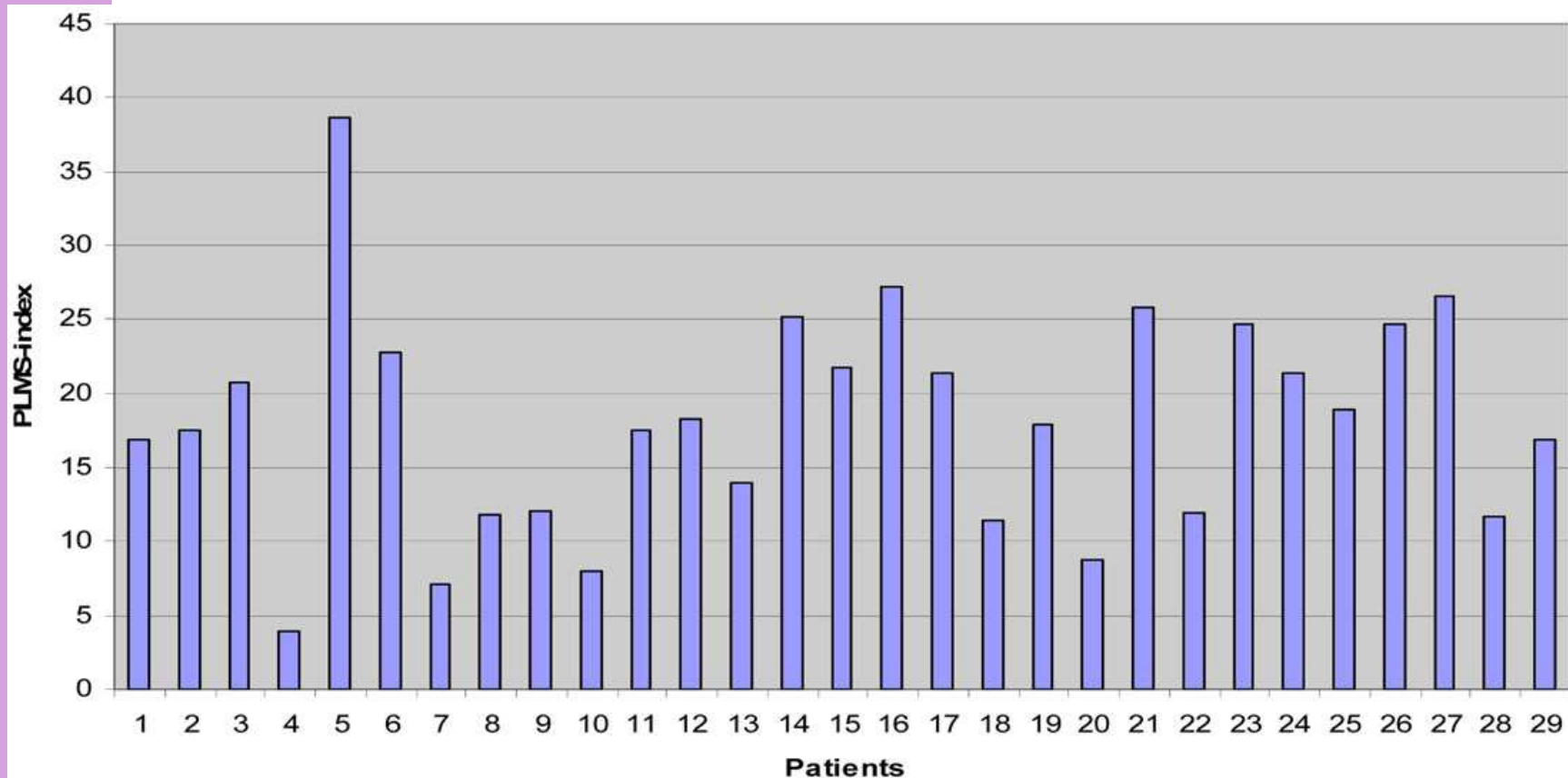
- Nocturnal polyuria
 - Natriuresis
 - Kaliuresis
 - Reduced dipping bloodpressure overnight
 - Higher renin aldosteron-levels
-
- Rittig, 2009 PhD Mahler, Kamperis 2010 Am J Phys Ren Phys

Nocturnal polyuria is associated with abnormal superficial sleep and restless legs syndrome (K Dhont Ghent, J Urology)

- **Disrupted sleep architecture in children:**
 - high incidence of PLMS
 - increased cortical arousability leading to awakening

- **Increased PLMS during sleep → frequently followed by cortical arousal**

Nocturnal polyuria is associated with abnormal superficial sleep and restless legs syndrome (K Dhont Ghent)



Association between nocturnal polyuria and OAB

➔ **J.Urology 2007 Vande Walle**

D. Baeyens (Ghent): Association of enuresis And ADHD = cognitive dysfunction

➔ **2004 J Urol**

- ➔ 15% of enuretic children: ADHD-COM
- ➔ 22.5%: ADHD-IA
- ➔ prevalence of ADHD higher in older children (9-12 vs 6-8y)
- ➔ mainly Nocturnal polyuria

➔ **2005 Acta Ped**

- ➔ 2y follow up prevalence
- ➔ 73% of ADHD diagnoses can be reconfirmed

D. Baeyens (Ghent): Association of enuresis And ADHD = cognitive dysfunction

➔ **2006 Acta Ped**

- ➔ Prevalence rate of ADHD is increased in an enuretic population compared to community samples
- ➔ Mainly nocturnal polyuria

➔ **2007 J Urol**

- ➔ 4y follow up prevalence
- ➔ 64% of ADHD diagnoses can be reconfirmed

D. Baeyens (Ghent): Association of enuresis And Prepulse inhibition

➤ 2006 J Urol

- brainstem inhibition deficit in children with enuresis (PPI)
- ADHD-IA: when additional attention is allocated to specific trials in the task, they fail to optimize sensory gating.
 - Enuresis + ADHD-IA: identification problem of bladder signals → inadequate/absent arousal effect

• 2007 J Urol

- ↻ 2y follow up brainstem inhibition
- ↻ no sign difference between enuresis and control group
 - brainstem maturation not associated with children becoming dry

D. Baeyens (Ghent): Association of enuresis And Prepulse inhibition

- **PPI = prepulse inhibition**
 - Measurement of attentional information processing

- **How? SEM (Startle Eyeblink Modification)**
 - PPI startle reflex

D. Baeyens (Ghent): Amelioration of ADHD coincides with amelioration of enuresis (J Urology)

Is this the rediscovery of the wheel?

- **If you had a bad night yesterday...**
 - Were you easy awake this morning ?
 - Were you not dizzy?, sleepy?, less concentrated?
 - Do you not want to have a nap this afternoon?
- **If you have a full bladder and my talk is to long**
 - Are you listening to me?
 - Are you concentrated?
 - Or are you looking to your watch?

conclusion

- **Enuresis nocturna is not a selflimiting “benign” disorder**
- **The potential psychological side-effects, but certainly the negative influence on cognitive functions**
 - Makes the wait and see attitude not longer defensible
 - Demands more effective treatment strategies, based on EBM, but targetting earlier in life
- **Comorbidity between enuresis / therapy-resistance / cognitive functions / sleepdisorders**