

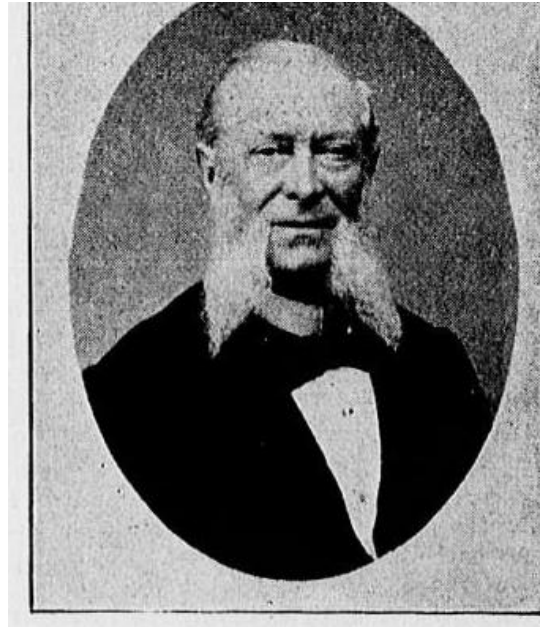
British Sleep Society 2015 Debate

The MSLT is an extremely important
and useful investigation in the
diagnosis of narcolepsy

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Narcolepsy

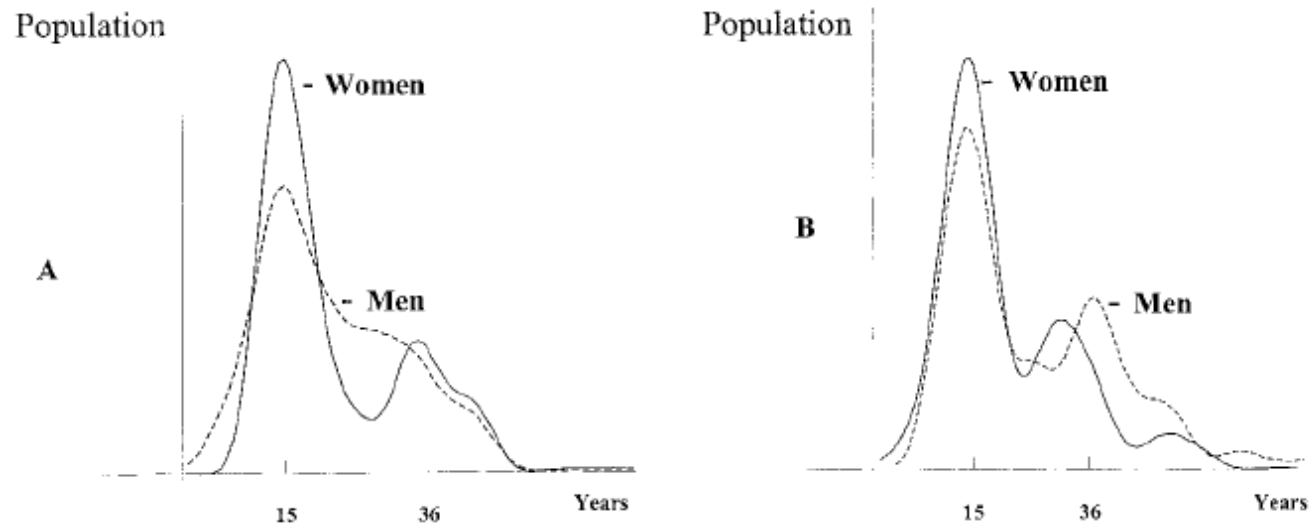
- Derived from the Greek
 - “Seized by somnolence”
- First named by a French neurologist, JBE Gelineau
 - Still known in certain centres as “Gelineau’s syndrome”
 - Earlier descriptions are noted from Carl Friedrich Otto Westphal



Frequency

- Prevalence is 25 to 50 per 100,000 with cataplexy
 - Longstreth et al, Sleep 2007, Vol 30 No1
- Incidence data is limited – possibly 1.37 per 100,000 person-years with or without cataplexy
 - Silber et al. Sleep 2002; 25:197-202
- Male to female ratio is 1:1
- Age of onset is variable
 - Two peaks – age 15 and 36
 - Dauvilliers et al. Neurology 2001, 57(11)

Age of onset



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Dauvilliers et al. Neurology 2001, 57(11)

Pathophysiology

- Frequently unrecognised
 - Typical delay of 1 to 61 years in diagnosis, around 10.5 years in UK
 - Morrish et al, Sleep Medicine 2004 (5)1 37-41
- 50% of adults report symptoms beginning as a teenager
- Can lead to impairment of social and academic performance

Morbidity

- Socially embarrassing, and source of “humour”
- Job impairment from sleep attacks, memory problems
- In one study, 24% of patients stopped working and 18% were fired
- Increased risk of death for automobile accidents
 - Cease driving on diagnosis until control is achieved
 - Permanent exclusion from Group 2



Assessment of Sleepiness

- Excessive daytime sleepiness is a significant, chronic problem
 - 5% of population
 - Lavie P. Sleep 1981 4(2): 147-58
 - Multiple causes
 - Morbidity for patient and those around
 - Mitler et al. Sleep 1988; 11(1):100-0
- Important to assess sleepiness accurately
- Rating scales have variable reliability
 - Epworth and Stanford Scales are subjective, other issues around use

Objective markers of sleepiness

- Initial studies used EEG changes to determine sleep onset
 - Davis et al Science 1937; 86: 448-50
- Evolved into Rechtschaffen and Kales scoring system
 - Sleep stages
 - Sleep latency
- Development of 90 minute day paradigm
 - Correlating sleepiness with sleep latency
 - 60 minutes wakefulness, 30 minute sleep
 - Using Stanford Sleepiness Scale and repeat measures of sleep latency
 - Carskadon and Dement Sleep 1982; 5 Suppl 2:S67-72

Does sleep latency exactly correlate with sleepiness?

- Tendency to sleep in the absence of alerting factors
- Sleepiness correlates with short sleep latency
 - Carskadon and Dement. Sleep 1982;5 Suppl 2: S67-72
- May also correlate with “sleepability”
 - Ability to transition into sleep
 - Some people have high sleepability without sleepiness
 - Harrison and Horne. Neurophysiol Clin. 1996; 26(1):15-20
- Influenced by multiple factors

Development of MSLT

- Six volunteers
 - 2 nights sleep deprivation
 - In bed every 2 hours and told to fall asleep
 - If awake, stopped after 20 minutes
 - Woken after one minute of stage 1
 - Prevent accumulation of sleep
- Proven correlation between deprivation and sleep latency
 - Carskadon and Dement Sleep Research 1977; 6:200.
 - Carskadon and Dement Percept Mot Skills 1979; 40(2):496-506
- SOREMPs in narcolepsy identified
 - Rechtschaffen A et al Electroencephalogr Clin Neurophysiol 1963, 15:599-609

MSLT in narcolepsy

- Recent review of 13 papers of MSLT in narcolepsy
 - Included control population in 4 studies
 - MSL for narcolepsy 3mins (+/- 3.1mins)
 - MSL for controls 10.5mins (+/- 4.6mins)
 - 84% of narcolepsy patients meet traditional limit of 5 minutes
- SOREMPs
 - 10 papers reviewed
 - Presence of cataplexy diagnostically sufficient
 - Majority of narcolepsy patients have SOREMPs
 - At least 2 or more
 - Frequency of SOREMPs increase with decreasing latency
 - Sensitivity of 0.78 and specificity of 0.93 for all studies,
 - Removing one study increased sensitivity to 0.79 and specificity to 0.98
- Studies reviewed by Arand et al Sleep 2005; 28(1):123-144

Guidance

- Difficulties in accessing sleep studies in UK
- Limited access

International Classification of Sleep Disorders (v2) state:

- while narcolepsy without cataplexy “must” be confirmed with polysomnography (PSG) and multiple sleep latency testing (MSLT), narcolepsy with cataplexy “should, whenever possible” be confirmed by PSG and MSLT
- Cataplexy thought to be virtually diagnostic of narcolepsy

Problems

- Symptoms of narcolepsy can occur in unaffected individuals
 - Sleep paralysis as isolated parasomnia in 50% of adult population
 - Excessive daytime sleepiness has broad differential diagnosis
 - Factitious narcolepsy and cataplexy have been described
- History dependent on experience of clinician

SHORT COMMUNICATION

Diagnosing narcolepsy with cataplexy on history alone: challenging the International Classification of Sleep Disorders (ICSD-2) criteria

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- Patients were identified over a 5 year period from the records in the Dept of Sleep Medicine
- All had been previously diagnosed as narcolepsy with cataplexy
- Referred for 2nd opinion as not responding to treatment

Case	Age (years)	Presenting symptoms	Medical history	Medication	PSG results	MSLT results	Urinary drug screen	HLA	Diagnosis and treatment
1	36	EDS with 3 hour daytime naps, unwitnessed "drop attacks", hypnagogic hallucinations, vivid dreams, sleep paralysis	Dyspepsia Treated prolactinoma	Cabergoline Esomeprazole Citalopram Loestrin	TST: 382.5 mins SE: 87.3% SL: 20mins REML: 67 mins AHI: 27 events/hr	No sleep recorded	-ve	-ve	OSAHS Trial of CPAP
2	34	EDS with 5-30 minute "sleep attacks", "drop attacks" when emotional or hungry, vivid dreams, hallucinations	Chronic fatigue syndrome, previous non-epileptic attacks	None	TST:247 mins SE: 53.3% SL: 13.5 mins REML: 78 mins AHI: 1.7 events/hr	MSL: 19.7 mins. Patient rolled eyes to simulate REM sleep. No REM	-ve	-ve	Did not attend follow-up or psychiatric review
3	48	EDS, "drop attacks" when emotional, hallucinations at sleep onset, sleep paralysis	None	None	TST: 384 mins SE: 77.4% SL: 27 mins REML: 182 mins AHI: 8.3 events/hr	No sleep recorded on 2 separate MSLT occasions	-ve	-ve	Refused to accept diagnosis, self-labelled as narcoleptic. Declined psychiatric review
4	37	EDS with daytime napping, loss of UL function when emotional, hypnopompic hallucinations, hallucinatory dreams, shouting and kicking whilst asleep, snoring and witnessed apnoeas	Anxiety and depression	Illegal use of amphetamines, GHB, clomipramine, clonazepam	TST: 374 mins SE: 77.5% SL: 16 mins REML: 11 mins AHI: 8.2 events/hr	MSL: 17.9 mins No REM	Cannabinoids	-ve	Cannabis abuse, poor sleep hygiene and depression. Reduce cannabis consumption
5	33	EDS with "sleep attacks" during the day, vague history of "drop attacks", sleep paralysis, vivid dreams and hallucinations	Insulin dependent diabetes mellitus, hypercholesterolaemia	Injectable insulin, simvastatin	TST: 356.5 mins SE: 75.7% SL: 30.5 mins REML: 119.5 mins AHI: 28 events/hr	MSL: 19.6 mins No REM	Cr not detectable; water substituted	-ve	OSAHS Trial of CPAP

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Investigations

- Exclude other causes
- HLA-DQB1*0602
 - 93% of patients with cataplexy and 56% without cataplexy
 - Mignot et al, Arch. Neurol 2000 59(10):1553-62
- MRI
 - Controversial. Suggestion that changes are visible in pons within the RAS
 - Structural abnormalities of brainstem is a differential of idiopathic narcolepsy

Other investigations

- Lumbar puncture
 - CSF hypocretin levels can also be checked, with low CSF hypocretin levels (less than 110pg/ml or 1/3 of the mean control value) are consistent with narcolepsy
 - Sensitivity 62%, specificity 98% in narcolepsy
 - Issues of diagnosis – not all patients had positive MSLT
 - Mignot et al, Arch. Neurol 2002 59(10):1553-62

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