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)
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Two peaks – age 15 and 36
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

• 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

I. Morrison\textsuperscript{a}, J. Bušková\textsuperscript{b}, S. Nevšimalová\textsuperscript{b}, N. J. Douglas\textsuperscript{c} and R. L. Riha\textsuperscript{c}

\textsuperscript{a}Department of Neurology, Institute of Neurological Sciences, Glasgow, UK; \textsuperscript{b}Department of Neurology, First Medical Faculty, Charles University, Prague, Czech Republic; and \textsuperscript{c}Department of Sleep Medicine, Royal Infirmary of Edinburgh, Edinburgh, UK

- 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 2\textsuperscript{nd} opinion as not responding to treatment
<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Presenting symptoms</th>
<th>Medical history</th>
<th>Medication</th>
<th>PSG results</th>
<th>MSLT results</th>
<th>Urinary drug screen</th>
<th>HLA</th>
<th>Diagnosis and treatment</th>
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<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>EDS with 3 hour daytime naps, unwitnessed “drop attacks”, hypnagogic hallucinations, vivid dreams, sleep paralysis</td>
<td>Dyspepsia Treated prolactinoma</td>
<td>Cabergoline Esomeprazole Citalopram Loestrin</td>
<td>TST: 382.5 mins SE: 87.3% SL: 20 mins REML: 67 mins AHI: 27 events/hr</td>
<td>No sleep recorded</td>
<td>-ve</td>
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<td>OSAHS Trial of CPAP</td>
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<td>2</td>
<td>34</td>
<td>EDS with 5-30 minute “sleep attacks”, “drop attacks” when emotional or hungry, vivid dreams, hallucinations</td>
<td>Chronic fatigue syndrome, previous non-epileptic attacks</td>
<td>None</td>
<td>TST: 247 mins SE: 53.3% SL: 13.5 mins REML: 78 mins AHI: 1.7 events/hr</td>
<td>MSL: 19.7 mins. Patient rolled eyes to simulate REM sleep. No REM</td>
<td>-ve</td>
<td>-ve</td>
<td>Did not attend follow-up or psychiatric review</td>
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<td>3</td>
<td>48</td>
<td>EDS, “drop attacks” when emotional, hallucinations at sleep onset, sleep paralysis</td>
<td>None</td>
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<td>TST: 384 mins SE: 77.4% SL: 27 mins REML: 182 mins AHI: 8.3 events/hr</td>
<td>No sleep recorded on 2 separate MSLT occasions</td>
<td>-ve</td>
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<td>Refused to accept diagnosis, self-labelled as narcoleptic. Declined psychiatric review</td>
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<td>Anxiety and depression</td>
<td>Illegal use of amphetamines, GHB, clomipramine, clonazepam</td>
<td>TST: 374 mins SE: 77.5% SL: 16 mins REML: 11 mins AHI: 8.2 events/hr</td>
<td>MSL: 17.9 mins No REM</td>
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<td>Insulin dependent diabetes mellitus, hypercholesterolaemia</td>
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<td>TST: 356.5 mins SE: 75.7% SL: 30.5 mins REML: 119.5 mins AHI: 28 events/hr</td>
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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 20002 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
The MSLT is an extremely important and useful investigation in the diagnosis of narcolepsy