# Diagnosing Narcolepsy in the Active Duty Military Population

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# Narcolepsy

- Narcolepsy type I and type II
  - Central hypersomnias
  - Manifested by excessive daytime sleepiness (EDS) and nocturnal sleep disruptions
  - 0.01-0.05% of the population worldwide [1,2]
- Narcolepsy type I
  - Cataplexy
  - Cerebrospinal fluid (CSF) hypocretin
- Narcolepsy type II
  - No pathognomonic symptoms or biomarkers


1. Dunne L, Patel P, et al. Misdiagnosis of narcolepsy. *Sleep Breath*. 2016; 20:1277-1284.
2. Cairns A, Bogan R. Prevalence of Clinical Correlates of a Short Onset REM Period (SOREMP) During Routine PSG. *Sleep*. 2015; 38(10):1575-1581.

# Diagnosis

- EDS
  - Daily periods of irrepressible need to sleep or daytime sleep lapses for at least 3 months[1]
- Polysomnography (PSG)
- Multiple sleep latency test (MSLT)
  - Sleep onset latency (SOL)
    - Mean 8 minutes or less
  - Sleep-onset REM periods (SOREMPs)
    - 2 or more (1 on PSG)

1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. *3rd* ed. Darien, IL: American Academy of Sleep Medicine; 2014.

# Diagnosis

- Diagnosis is challenging
  - As many as 50% of patients may be misdiagnosed[1]
- False positives on MSLT
  - SOREMPs can be caused by medication withdrawal, medical conditions, and multiple sleep disorders[2,3]
- High prevalence of sleep disorders in military personnel[4,5]


1. Dunne L, Patel P, et al. Misdiagnosis of narcolepsy. *Sleep Breath*. 2016; 20:1277-1284.
2. Aldrich M, Chervin R, Malow B. Value of the multiple sleep latency test (MSLT) for the diagnosis of narcolepsy. *Sleep*. 1997; 20(8):620-629.
3. Murer T, Imbach L, et al. Optimizing MSLT Specificity in Narcolepsy with Cataplexy. *Sleep*. 2017; 40(12):1-9.
4. Mysliwiec et al. Sleep Disorders and Associated Medical Comorbidities in Active Duty Military Personnel. Sleep 2013; 36(1):167-174.
5. Luxton D, Greenburg D, Ryan J, Niven A, Wheeler G, & Mysliwiec V. (2011). Prevalence and impact of short sleep duration in redeployed OIF soldiers. *Sleep*, *34*(9), 1189-1195.

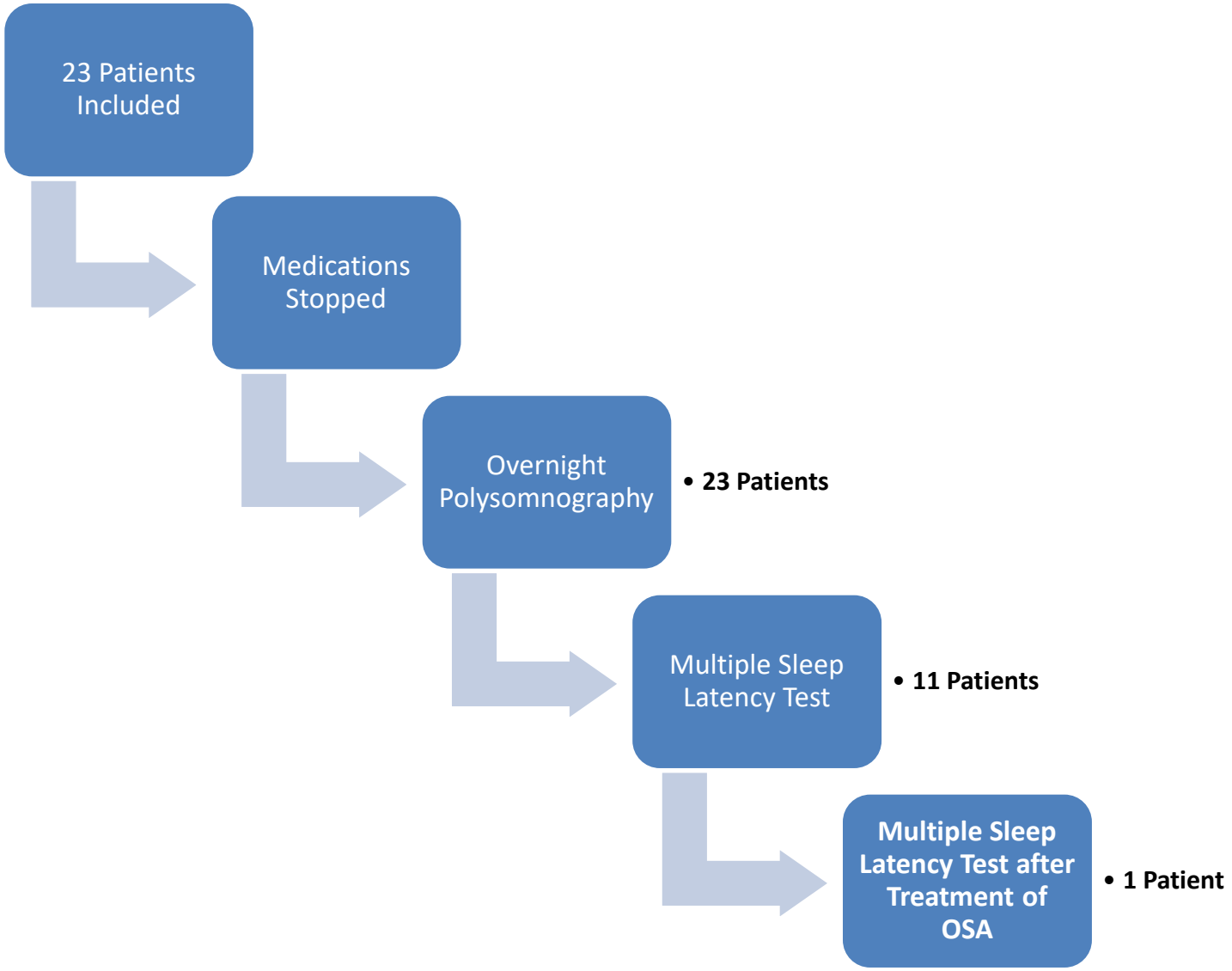
# Question

- Diagnostic testing for narcolepsy may be influenced by the presence of comorbid sleep disorders including sleep-disordered breathing, insufficient sleep duration, and circadian misalignment which are common in active military personnel.
  - How many patients previously diagnosed with narcolepsy, referred for repeat diagnostic evaluation will retain their diagnosis or be diagnosed with a confounding sleep disorder?

# Methods

- Inclusion criteria
  - Patients age 18-65
  - Previous diagnosis of narcolepsy (either type I or type II) made at an outside facility
  - Decision to repeat diagnostic testing
  - Minimum of 7 days of interpretable actigraphic data on repeat testing
- Exclusion criteria
  - Initial work up and diagnosis at the Wilford Hall Ambulatory Surgical Center Sleep Disorder Center
  - History of sleep disordered breathing
  - Absence of 7 days of interpretable actigraphic data on repeat testing

# Methods


23 Patients Included
Medications Stopped
Overnight Polysomnography
• 23 Patients
Multiple Sleep Latency Test
• 11 Patients
Multiple Sleep Latency Test after Treatment of OSA
• 1 Patient

# Results

**Table 1. Original Polysomnography and MSLT Data.**

| Patient | AHI (events/hr) | Sleep Onset Latency (min:sec) | SOREMPs (#) |
|---|---|---|---|
| 1 | 1.9 | N/A | N/A |
| 2 | N/A | 1:18 | 4 |
| 3 | 0.4 | 5:06 | 4 |
| 4 | 0.4 | N/A | N/A |
| 5 | 0.5 | 2:37 | 2 |
| 6 | 1 | 6:24 | 4 |
| 7 | 1.3 | 2:04 | 2 |
| 8 | 0.1 | 7 :00 | 2 |
| 9 | 1.1 | N/A | N/A |
| 10 | 0.3 | 2:54 | 2 |
| 11 | N/A | 3:00 | 2 |
| 12 | 3 | 4:36 | 3 |
| 13 | 0.4 | 2:18 | 3 |
| 14 | 0 | 6:00 | 2 |
| 15 | N/A | 3:03 | 3 |
| 16 | 0.8 | 3:36 | 2 |
| 17 | 1.7 | 6:18 | 2 |
| 18 | N/A | 2:00 | 2 |
| 19 | 4.1 | 0:22 | 2 |
| 20 | 1.5 | 2:24 | 3 |
| 21 | 0 | 6:30 | 2 |
| 22 | 0.8 | 1:24 | 4 |
| 23 | 1:1 | 3:00 | 2 |

Table Results presented as time (min:sec) or number. N/A indicates that results were unavailable

**Table 2. Baseline Demographics and Polysomnography Results (N=23)**

| | |
|---|---|
| Age | 35.0 ± 11.3 years |
| Male, no. | 14 (60.7%) |
| Female, no. | 9 (39.1%) |
| BMI | 27.7 ± 3.2 kg/m$^2$ |
| History of cataplexy, no. | 4 (17.4%) |
| Mood disorder, no. | 6 (26.1%) |
| Sodium oxybate prescription, no. | 6 (26.1%) |
| Stimulant prescription, no. | 18 (78.3%) |
| SSRI/SNRI prescription, no. | 3 (13.0%) |
| Sleep onset latency | 22 ± 26.0 min |
| Wake after sleep onset | 39 ± 16.8 min |
| Arousal index | 17 ±7.17 events/hr |
| Total sleep time | 405 ± 50.7 min |
| Sleep efficiency | 87 ± 7% |
| REM latency | 123 ± 80.3 min |
| N1 | 7.3 ± 4.5% |
| N2 | 54.8 ± 6.5% |
| N3 | 18.4 ± 5.8% |
| REM | 19.5 ± 6.4% |
| AHI | 5.0 ± 3.9 events/hr |
| REM AHI | 10.6 ± 10.1 events/hr |
| Supine AHI | 10.6 ± 11.2 events/hr |
| Left lateral AHI | 3.3 ± 3.9 events/hr |
| Right lateral AHI | 2.2 ± 2.5 events/hr |
| SpO2 nadir | 90.3 ± 3.0% |

Results presented as mean ± SD or number (%).
BMI = Body Mass Index.

# Results

**Table 3. Actigraphy Results**

| Patient | Total Sleep Time (Min) | Sleep Onset Latency (Min) | Bedtime | Wake Time | Time in bed (min) | Sleep Efficiency (%) |
|---|---|---|---|---|---|---|
| 1 | 366 | 9 | 2:37 | 10:16 | 458 | 80 |
| 2 | 330 | 3 | 0:13 | 6:19 | 366 | 90 |
| 3 | 394 | 5 | 22:51 | 6:39 | 467 | 84 |
| 4 | 401 | 29 | 23:51 | 8:12 | 501 | 80 |
| 5 | 312 | 20 | 22:00 | 4:51 | 411 | 76 |
| 6 | 442 | 11 | 22:41 | 7:39 | 537 | 82 |
| 7 | 353 | 18 | 0:46 | 7 :55 | 428 | 82 |
| 8 | 477 | 11 | 22:12 | 9 :27 | 567 | 84 |
| 9 | 423 | 4 | 22:57 | 7:14 | 497 | 85 |
| 10 | 362 | 15 | 22:41 | 5:41 | 420 | 87 |
| 11 | 388 | 19 | 18:02 | 2:26 | 503 | 79 |
| 12 | 448 | 3 | 23:14 | 7:58 | 524 | 86 |
| 13 | 436 | 1 | 22:33 | 6:56 | 502 | 87 |
| 14 | 431 | 24 | 22:46 | 7:26 | 520 | 82 |
| 15 | 579 | 14 | 22:36 | 8:16 | 579 | 75 |
| 16 | 350 | 6 | 0:08 | 7:45 | 456 | 74 |
| 17 | 420 | 8 | 23:38 | 7:52 | 494 | 85 |
| 18 | 349 | 9 | 1:12 | 8:23 | 430 | 79 |
| 19 | 471 | 14 | 1:19 | 10:14 | 534 | 88 |
| 20 | 493 | 15 | 21:06 | 6:33 | 566 | 87 |
| 21 | 492 | 28 | 21:51 | 7:30 | 579 | 85 |
| 22 | 378 | 4 | 0:49 | 8:21 | 451 | 84 |
| 23 | 424 | 3 | 20:39 | 4:51 | 491 | 84 |
| Mean: | 409 ± 53 min | 12 ± 8 min | 23:04 ± 22 min | 7:20 ± 45 min | 491± 57 min | 83 ± 4% |

Results presented as average over 14-day actigraphy. Time presented as 24-hour clock.

# Results

**Table 4. Multiple Sleep Latency Test Results and Final Diagnosis**

| Patient | Mean Sleep Onset Latency (min: sec) | Number of SOREMPs (#) | Final Diagnosis |
|---|---|---|---|
| 1 | N/A | N/A | DSWPD |
| 2 | N/A | N/A | Mild OSA (supine predominant: AHI: 6.8, supine AHI: 31.1)*;insufficient sleep syndrome** |
| 3 | 7:18 | 0 | Insufficient sleep syndrome |
| 4 | N/A | N/A | Mild OSA (supine predominant: AHI: 10.7, supine AHI: 31.3); insufficient sleep syndrome |
| 5 | N/A | N/A | Mild OSA (supine predominant: AHI: 13.2, supine AHI: 16.8); insufficient sleep syndrome |
| 6 | 9:39 | 3 | Narcolepsy without cataplexy |
| 7 | N/A | N/A | Insufficient sleep syndrome |
| 8 | 12:21 | 0 | Negative work-up*** |
| 9 | N/A | N/A | Irregular sleep/wake times**** |
| 10 | N/A | N/A | Insufficient sleep syndrome |
| 11 | N/A | N/A | Mild OSA (supine predominant: AHI: 6.3, supine AHI: 30.2); Irregular sleep/wake times |
| 12 | N/A | N/A | Mild OSA (AHI: 12.4); Irregular sleep/wake times |
| 13 | 6:51 | 1 | Narcolepsy without cataplexy |
| 14 | 7:10 | 0 | Idiopathic hypersomnia |
| 15 | 15:39 | 0 | Negative work-up |
| 16 | N/A | N/A | Insufficient sleep syndrome |
| 17 | 10:11 | 0 | Subjective hypersomnia NOS |
| 18 | N/A | N/A | Mild OSA (AHI: 9.7); insufficient sleep syndrome |
| 19 | 5:46 | 0 | Irregular sleep/wake times |
| 20 | 3:03 | 0 | Mild OSA (AHI: 7); Hypersomnia |
| 21 | 11:16 | 0 | Insufficient sleep syndrome/Subjective hypersomnia |
| 22 | 7:19 | 0 | Mild OSA (AHI: 7.6); insufficient sleep syndrome |
| 23 | 1:25 | 0 | Mild OSA (AHI: 7.5) |
| Mean: | 8: 10 (± 3:56) | | |

N/A indicates test was not performed.

SOREMP = sleep onset REM period. DSWPD = delayed sleep-wake phase disorder.
*Average of less than 7 hours per night on actigraphy.

**AHI > 5 events/hour with supine AHI at least twice lateral AHI.

***Normal work-up without objective criteria for diagnosis.

****Per clinician interpretation of actigraphy; characterized by significant variability in bed time and wake times.

# Discussion

- The majority of patients (91%) in this study did not meet the diagnostic criteria for narcolepsy on repeat testing
  - Insufficient sleep syndrome (43%)
  - OSA (39%)
  - Circadian rhythm sleep-wake disorders (21%)
- Actigraphy recommended but not required[1]
- Obstructive Sleep Apnea
  - Supine predominate or mild OSA and the first night effect can complicate diagnosis[2,3]


1. Smith MT, et al. (2018) Use of Actigraphy for the Evaluation of Sleep Disorders and Circadian Rhythm Sleep-Wake Disorders: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. Journal of Clinical Sleep Medicine 14:1209-1230.
2. Guilleminault C, Stoohs R, Clerk A, Cetel M, Maistros P (1993) A Cause of Excessive Daytime Sleepiness. The Upper Airway Resistance Syndrome. Chest 104:781-787
3. Skiba V, Goldstein C, Schotland H (2015) Night-to-Night Variability in Sleep Disordered Breathing and the Utility of Esophageal Pressure Monitoring in Suspected Obstructive Sleep Apnea. Journal of Clinical Sleep Medicine 11:597-602.

# Conclusion

- Narcolepsy type I and type II
  - Rare disorders
  - Diagnostically challenging
- High prevalence of sleep disorders in the military population
- Confounding sleep disorders are common
  - PSG
  - Actigraphy

# Questions?