MEASURING IMPAIRMENT: VALIDATED METHODS FOR ASSESSING SEDATING MEDICATIONS

Gary G. Kay, Ph.D.
Associate Clinical Professor of Neurology
Director, Neuropsychology Division
Georgetown University School of Medicine
Washington, DC
&
President
Washington Neuropsychological Institute
Washington, DC

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Attitudes & Use of Sedating OTC Medications

- Public shows little awareness of the risks of using common sedating OTC medications
- Public believes that if you aren't drowsy you aren't sedated

Definition of Sedation

- Depression of brain functioning by a medication, manifested by:
  - sleepiness, drowsiness, fatigue
  - slowed brain activity
  - reduced wakefulness
  - impaired performance

Methods for Evaluating Sedation

- Self-report measures
- Physiologic measures
- Performance measures

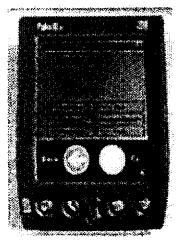
Evaluating Sedation: Self-Report Methods

- ❑Diary Cards
- ❑Rating Scales, Mood Inventories
- ❑Visual Analog Scales
- ❑Personal Data Assistant (e.g., Palm Pilot)
- ❑Prescription Event Monitoring

Real-Time Measurement of Personal Experience

- High subject compliance
- Time-logging of entries
- Improved data handling

Superiority to paper diary demonstrated in recent SUNY study (Shifman et al., 2001)



Limitations of Self-Report Measures

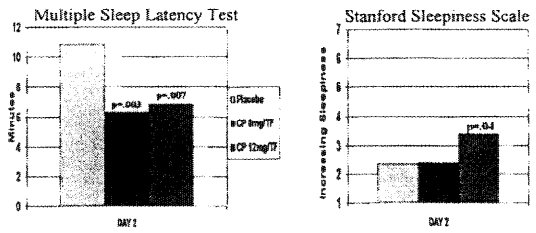
- Subjectivity
- Biased reporting
- Poor diary compliance
- Low agreement with physiological and performance measures
  - self-reported sleepiness fails to reflect physiological sleepiness[1]
  - self-reported sleepiness fails to reflect cognitive performance deficit[2]
  - self-reported sleepiness fails to reflect driving performance[3]

1. Kay GG, Plotkin KE, Quig MB, et al. *Am J Man Care*. 1997;3:1843-1848.
2. Yasuda S, Zannikos P, Kay G, et al (submitted for publication; Nov 2001)
3. Weiler JM, Bloomfield JR, Woodworth GG, et al. *Ann Intern Med*. 2000;132:354-63.

Evaluating Sedation: Physiologic Measures

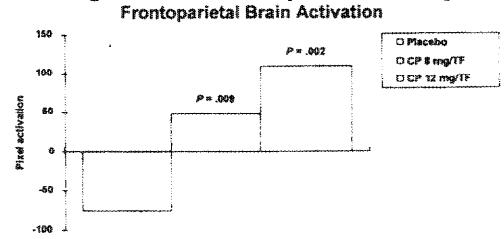
- EEG (e.g., continuous EEG for microsleeps)
- Evoked potentials (e.g., P300)
- Functional brain imaging (e.g., PET and fMRI)
- Multiple sleep latency test (MSLT)
- Activity monitors (e.g., wrist actigraph)

Effect of Evening Chlorpheniramine and Morning Terfenadine (AM/PM Dosing)

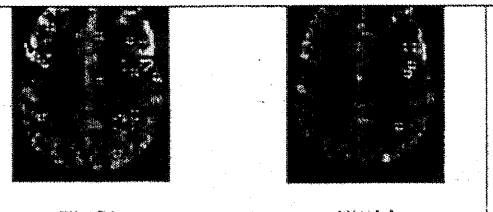


1. Kay GG, Plotkin KE, Quig MB, et al. *Am J Man Care*. 1997;3:1843-1848

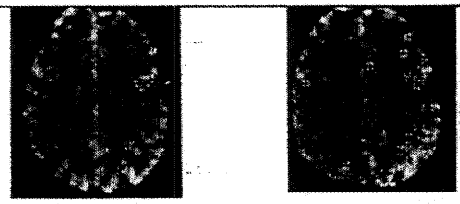
Functional MRI: Mental Arithmetic Test



Starbuck et al., Human Psychopharmacology, 2000



Starbuck et al., Human Psychopharmacology, 2000



Starbuck et al., Human Psychopharmacology, 2000

Evaluating Sedation: Performance Measures

- Cognitive testing
- Psychomotor testing
- Simulation (e.g., driving, flying)

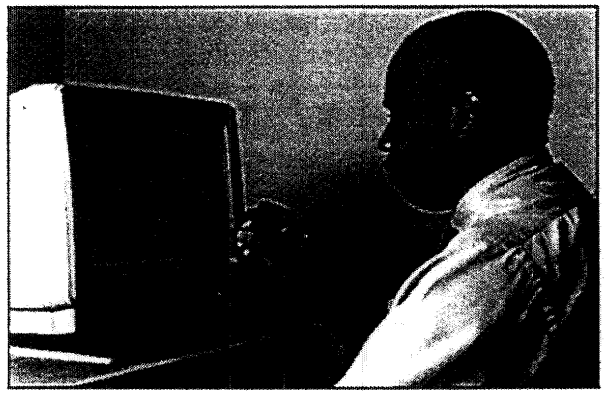
Characteristics of Computerized Neuropsychological Tests

- Standardized instructions and stimulus presentation
- Enhanced sensitivity to detect neuro-cognitive and psychomotor changes
- Highly accurate measurement of speed and accuracy
- Designed for repeated administration
- Predictive of performance of real-world activities (e.g., flying)

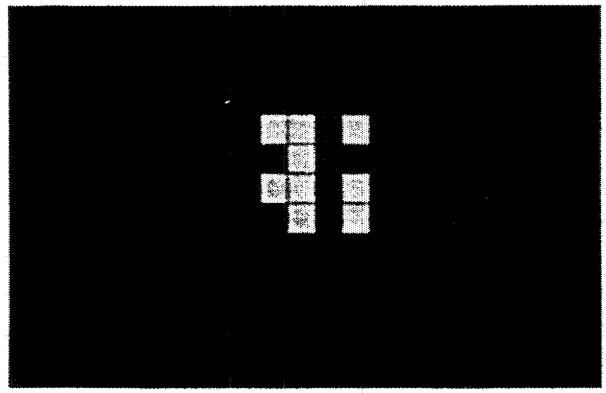
Kane & Kay, Neuropsychology Reviews, 1997

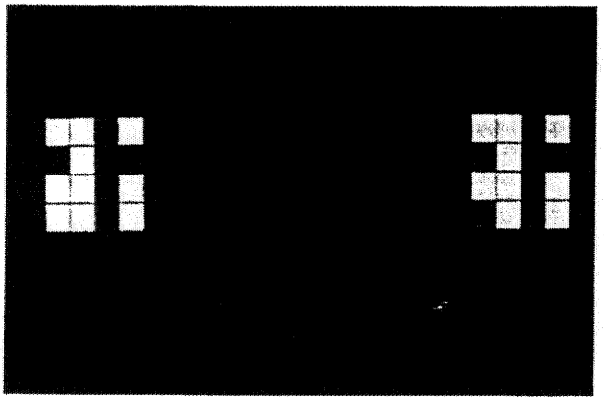
PHARMACEUTICAL RESEARCH EMPLOYING CogScreen®

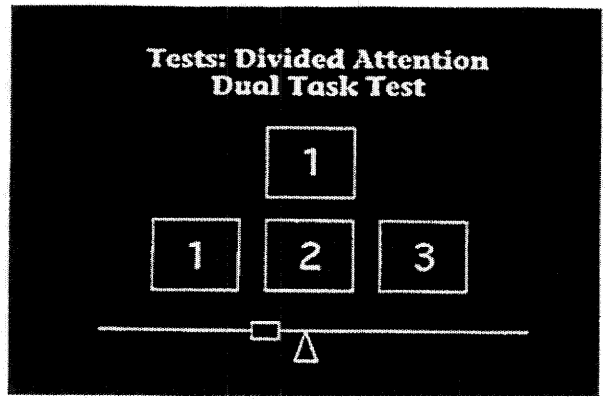
- ANTIHISTAMINES (DOD, FDA, Pharma)
- ANTIHYPERTENSIVES (FAA)
- NUTRASWEET (FAA/FDA)
- CHOLESTEROL LOWERING MEDICATIONS (Pharma)
- ORAL DIABETES MEDICATION (Pharma)
- HORMONE REPLACEMENT THERAPY (Pharma)
- ANTIBIOTICS (Pharma)



Computerized Neuropsychological Testing of Performance



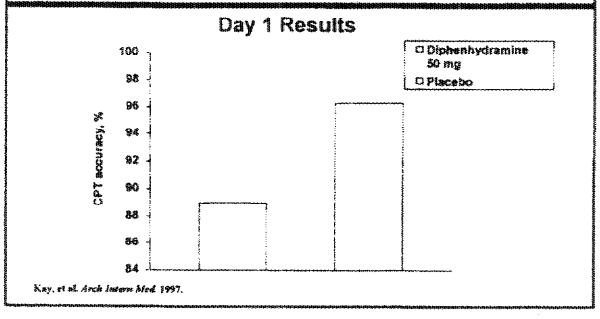




CRITICAL COGNITIVE DOMAINS FOR DEMONSTRATING SEDATION

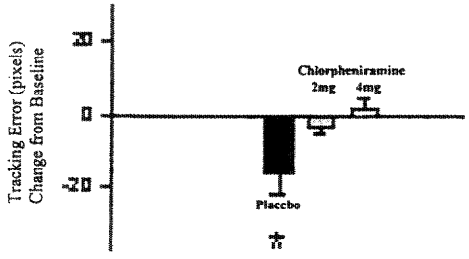
- **VIGILANCE:** Capacity to sustain attention under conditions of minimal arousal (e.g., monotonous tasks)
- **DIVIDED ATTENTION:** Ability to perform simultaneous mental activities (especially tracking)
- **WORKING MEMORY:** Ability to hold information temporarily in one's head for purposes of using the information in a calculation, or other mental activity

Vigilance: Kay Continuous Performance Test



CogScreen Dual Task Tracking Test

Acute dosing - 7 hours post dosing; Mean SSS < 2



Yasuda, Zannikos, Kay, Fried, & Wainer, 2001

Summary

- Sedating medications can cause impairment in the absence of sleepiness.
- Sedating effects may carry over to the following day even when medications are taken at night.
- Functions most vulnerable to sedating medications are: vigilance, psychomotor skills under divided attention conditions, and working memory.
- Reliable and valid measures are currently available for evaluating the self-report, physiological and performance effects of medications.