Importance of Training and Quality Control of Post-Operative Delirium Assessment:

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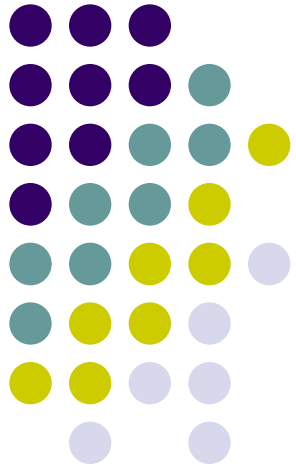


Disclosure

- **Current funding:**
  - **Relevant:**
    - **R01 MH085740 (NIH/NIMH: PI Lee HB)**
    - **R01AG029656 (NIH/NIA: PI Silverstein J)**
    - **P30 DK34989 (NIH/NIDDK: Yale Liver Center Pilot Grant: PI: Lee HB)**
  - **Unrelated: RLS Foundation Research Grant** (PI: LEE HB)
- **Other financial relationships:** None

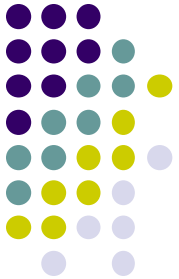
Outline

- Briefly describe a geriatric/CL psychiatrist's perspective on difficulty in diagnosis of delirium.

- Describe three post-surgical delirium prevention trials and compare their training and quality assurance protocols.
  - Focus Cognitive Ancillary Study (PI: Gruber-Baldini)
  - STRIDE study (PI: Sieber)
  - Dexlirium Study (PI: Silverstein)

- Describe strengths and limitations of each method while focusing on pitfalls.

Why delirium diagnosis challenging for a psychiatrist as well.



- **1. Delirium is a longitudinal diagnosis**
  - Lack of pre-morbid level of cognition or function
  - “Acute” versus “Gradual” change.
- **2. Symptoms of delirium commonly overlaps with symptoms of other psychiatric conditions (e.g. dementia and depression).**
  - 46% of patients with delirium were misdiagnosed by the referring service personnel (Armstrong 1997)
  - 42% of “depression” referral were delirious (Farrel, 1995)
- **3. “Hardest diagnosis in psychiatry”:**
  - Milder, hypoactive delirium superimposed on dementia.

Change of Diagnostic Criteria in DSM

- DSM III (1980)
- DSM III-R (1987)
- DSM IV (1990)
- DSM V (2013)
- Depending on the definition, prevalence rates differ substantially (Liptzin 1991, Cole 2003, Laurila et al, 2003)
  - Of 230 geriatric hospital patients, prevalence varied depending on criteria:
  - DSM-IV (24.9% of the subjects) followed by DSM-III-R (19.5%), DSM-III (18.8%) and ICD-10 (10.1%).

Using CAM to make diagnosis of Delirium (Laurila, 2002)

- 81 consecutive elderly patients in geriatric hospital
- Sensitivity rates of the CAM were proved to be only moderate (0.81–0.86) against all DSM criteria of delirium. The specificity rates were lower (0.63–0.84).
- CAM defines delirium in its own way and, ironically and probably provides the most **enduring and generalizable** diagnostic outcome.

Table 5. Sensitivity and specificity rates, positive and negative predictive values, and positive and negative likelihood ratios of CAM compared to DSM-III, DSM-III-R, DSM-IV, and ICD-10 as reference standards

	DSM-III		DSM-IIIR		DSM-IV		ICD-10	
	+	−	+	−	+	−	+	−
Positive CAM score	17	17	17	17	26	8	8	26
Negative CAM score	3	44	4	43	6	41	2	45
Sensitivity rate	0.85		0.81		0.81		0.80	
Specificity rate	0.72		0.72		0.84		0.63	
Positive predictive value	0.50		0.50		0.76		0.24	
Negative predictive value	0.94		0.91		0.87		0.96	
Likelihood ratio for a positive test	3.05		2.86		4.98		2.18	
Likelihood ratio for a negative test	0.21		0.27		0.22		0.32	

Use of CAM in PSD clinical trials

- Most of post-surgical delirium prevention trials utilizes CAM
  - Nearly 100%, if secondary outcomes.
- Why CAM in PSD studies?
  - Generalizable.
  - Validity is well-established
  - “Simplicity, ” however, rigorous training is essential.
    - Minimally trained bedside nurses – 23.8% and 66.7% sensitivity based on two scoring methods for CAM (Lemiengre et, JAGS 2006)
    - Partially trained research nurses – 13% detection (Rolfson, IJP 1999)

“Myth of Simplicity”

- Wong CL,et al. JAMA 2010; 304:779-786
  - CAM has the best available supportive data as a bedside delirium instrument (summary-positive LR, 9.6; 95% CI, 5.8-16.0; summary-negative LR, 0.16; 95% CI, 0.09-0.29).”
  - Conclusion: “The choice of instrument may be dictated by the amount of time available and the discipline of the examiner; however, **the best evidence supports use of the CAM, which takes 5 minutes to administer**.”
  - “…But how long does it take to get to CAM?”

But, how long does it take to GET TO CAM?

- Gathering information for each component of CAM takes time and clinical judgment
  - Acute cognitive change – testing, review of records,
  - Attention – testing cognition
  - Disorganized thought – interview with the patient
  - Level of consciousness – observation of the patient

- **Delirium Diagnosis Methodology Used by Reference Raters in Research: A Survey-Based Study (Neufeld KJ, et al, under review)**
  - 33 of 39 studies from 3 recent systematic reviews of delirium detection instruments.
  - Tremendous variability in diagnostic methods and rater backgrounds

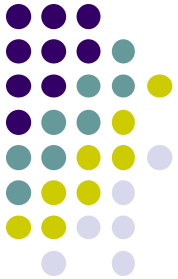
Tremendous variability in incidence of acute post-hip fracture delirium with CAM: 5 – 40% (Bruce 2006)

AUTHORS	SETTING	EXCLUDED COGNITIVE IMPAIRMENT	AGE (YEARS)	N	RATING SCALE	POSTOP DAYS TESTED	INCIDENCE	95% CI
Johansson *et al.* 2002	Örebro County Hospital, Sweden	No	Mean = 80.4	47	NEECHAM	Day 7	4%	0.74–15.7%
Brauer *et al.* 2000	Four New York hospitals	No	Median = 85	546	CAM	5 days/week	5.30%	3.6–7.6%
Edlund *et al.* 1999	Pitea River Valley Hospital, Sweden	No	Mean = 77.1	44	DSM-IIIR/ OBS	Daily	11.40%	4.3–25.4%
Morrison *et al.* 2003	Four New York hospitals	No	Not stated	525	CAM	5 days/week	14.00%	11.2–17.1%
Schuurmans *et al.* 2003	General hospital, Netherlands	No	Mean = 82.7	92	DSM-IV	Daily for 6 days	19.60%	12.3–29.4%
Edlund *et al.* 2001	University Hospital, Umeå, Sweden	No	Mean = 79.5	71	DSM-IV/OBS	Daily	26.80%	17.3–38.8%
Formiga *et al.* 2003	Two university hospitals, Barcelona	No	Mean = 92.4	89	CAM	Day 1 or 2, and at discharge	28.10%	19.3–38.8%
Gustafson *et al.* 1988	University Hospital, Umea, Sweden	No	Mean = 79.3	74	DSM-III/OBS	Daily	41.90%	30.7–53.9%
Zakriya *et al.* 2004	Medical Centre, U.S.A.	No – all had dementia	Mean = 78–79	10	CAM	Daily	50%	20.1–79.9%
Thakur *et al.* 2002	Community teaching hospital, U.S.A.	No	Range = 66–98	30	CAM	Not given	53.30%	35.4–71.2%
Kagansky *et al.* 2004	Community teaching hospital, Israel	Excluded severe dementia	Mean = 82	96	CAM/DRS	Day 7	6.30%	2.6–13.6%
Andersson *et al.* 2001	Lund County City Hospital, Sweden	Confusional states excluded	Range = 65–96	208	DSM-IV/OBS	Daily	20.20%	14.7–25.6%
Duppils *et al.* 2000	County hospital, Sweden	Dementia and MMSE $\leq$ 10 excluded	65+	149	DSM-IV	At least twice daily	24.30%	17.4–31.2%
Zakriya *et al.* 2002	Medical Centre, U.S.A.	Dementia excluded	Mean = 77.6	168	CAM	Day 2 until discharge	28.00%	21.2–34.8%
Galanakis *et al.* 2001	Munich hospital, Germany	Severe dementia excluded	Mean = 74.9	37	CAM	Days 1–7	40.50%	24.7–56.3%
Bowman 1997	Manitoba teaching hospital, Canada	Dementia and MMSE $\leq$ 23 excluded	Mean = 80	17	DSM-III	Days 1–5, twice daily	47.10%	23.4–70.8%

Importance of Case Ascertainment methods in Delirium Prevention or Treatment Trials

- Treatment Trials
  - Recruitment of delirious study subjects
    - Under-detection: Cannot run the trials
    - Over-detection: Weakened signal of intervention by recruiting wrong subjects
- Prevention Trials:
  - Primary outcomes: Delirium
    - Under-detection: Need a large sample size
    - Over -detection: Results in eronneously negative or positive findings
- Must balance practicality and science based on available personnel, setting, and budget.

Lessons from Three NIA-sponsored Post-Surgical Delirium Prevention Trials.



- Focus Cognitive Ancillary Study (PI: Gruber-Baldini)
  - Completed – my role: peripheral involvement.
- STRIDE study (PI: Sieber)
  - On-going - designed the study outcomes/ training protocol/ quality assurance while at Hopkins
- Dexlirium Study (PI: Silverstein)
  - Ongoing – primary delirium “expert”- responsible for training and quality assurance.

Summary

	Focus Cognition	Dexlirium	STRIDE
Sample size	139	708 (planned)	200
Site #	17	7	1
Intervention	Transfusion	Dexmedotimidine	Sedation Level
Instruments	DIS, MDAS, CAM	DIS, MDAS, CAM	DRS-98, CAM, DI
Training	Web-based certification and limited in-person training in the beginning.	Web-based/ supplemented by in-person at each site by coordinating center	Fully in-person
Quality Assurance	Weekly Teleconference	Teleconference and monthly case presentation and data review	Consensus Panel Case presentation

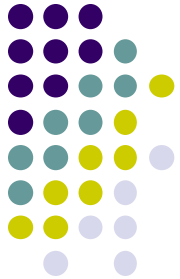
FOCUS Cognitive Ancillary Study (PI: Ann Gruber-Baldini)

- Goal: To examine the impact of the hemoglobin interventions on delirium in a subsample of 200 subjects (100 per randomization group).
- Reality: 17 sites and short duration of intense recruitment.
  - Must weigh the issue of fidelity and practicality of outcome measure (delirium: case versus severity)
  - Need for multiple raters in multiple sites
    - Cannot utilize clinical psychiatrists for all sites
    - Alternative: Train available research staff (including non-clinical Research Assistants)
      - Delirium Symptom Interview (structured)
      - Memorial Delirium Assessment Scale (severity)
      - Confusion Assessment Method – primary outcome (case)

FOCUS Cognitive Study: Training and Quality Assuranance

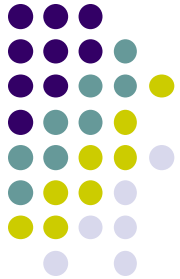
- Training:
  - Investigator kick-off meeting
  - Introductory lectures and training
  - Certification: Web-based training – certification process -3 video cases
  - Individual ratings of DSI, MDAS and CAM submitted to the coordinating site for Case #3
  - Case #3 answers are compared to the master answers with individual feedback.
- Quality Assurance
  - Site visits and teleconference

FOCUS Cognitive Study: Strengths and limitations



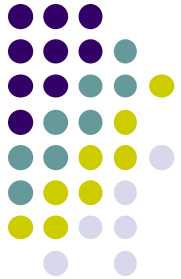
- Balancing fidelity and practicality
  - Wide range of raters (physicians, nurses, non-clinical RAs)
    - What is the “gold standard”?
  - Web-based training has its strengths and weaknesses
    - Covers multiple sites distributed widely in geography
    - Cannot provide close oversight over the training
    - RA turnover is difficult to overcome
  - However, for multi-site clinical trial of short duration and limited budget, probably no other choice.

A Strategy to Reduce the Incidence of Post-Operative Delirium in Elderly patients: The STRIDE Study (PI: Frederick Sieber)



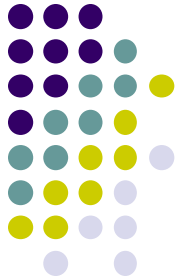
- Sponsor: NIA
- Design: Single-site randomized double-blinded clinical trial.
- Aim: to determine whether limiting the **level of sedation** in elderly patients during spinal anesthesia for surgical repair of a hip fracture will lead to a lower rate of post-operative delirium.
- Intervention: To give one group of elderly traumatic hip fracture patients standard spinal anesthesia, with light-to-moderate sedation, and the other group standard spinal anesthesia with deeper sedation.

STRIDE Study: Training and QA



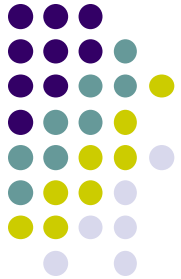
- Single site study with experienced research nurses as the rater.
- CL Psychiatrist trainer is on-site and available at all times.
- Introductory Group Seminar – 6+ hours to go over the manuals for CAM and DRS-98.
- In person training – three practice cases prior to data collection.
- Bi-weekly case presentation by the Research RN to the consensus panel.
  - Multi-disciplinary consensus panel consists of psychiatrist, geriatrician, anesthesiologist, and surgeon.

STRIDE Study:
Strengths and limitations



- Single-site design allows more rigorous training protocol and quality assurance.
- high personnel cost for rater/trainer/consensus panel.
  - Consensus Panel blind to the group assignment affords more “gold-standard”-like comparison.
  - Took a long lead-in time.
- Consensus panel methods “adapted” from other dementia prevention studies.

Dexlirium Study (PI: Jeff Silverstein)



- Sponsor: NIA -
- randomized double blinded, parallel group, placebo-controlled study of the effects of perioperative dexmedetomidine on the incidence of postoperative delirium and postoperative cognitive dysfunction
- Sites: 8 sites
- Duration: “5 years”
- Target sample: 706 elderly patients undergoing elective “major” general surgery under general anesthesia
- dexmedetomidine vs. placebo

Dexlirium Study: before QA

- Limitation imposed by the multi-site study design and limited personnel and budget.
  - Also, rapid turnover of raters
- Similar to Focus Cognitive Study – Wide range of clinical background among the raters: "non-clinical" RA to nurses and MDs.
- Formal training and QA protocol was implemented in the middle of the study
  - Concern about low delirium incidence

Dexlirium Study: Training and QA

- RAs asked to read the protocol manuals and go through the web-based certification process first.
- 3 video cases from the FOCUS cognition study
- Site visits by PI and Delirium Trainer
- Monthly teleconference with delirium assessment case presentation from each site.
- Data review of every delirium assessment by the neuropsychiatrist for detection of data inconsistency and data reconciliation.

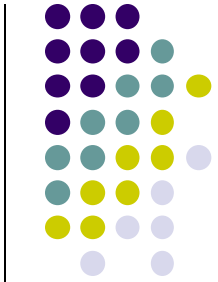
Detection of incident delirium before and after QA program

- Unpublished data

Delirium Incidence before and after QA implemented

- Unpublished data

Dexlirium Study: Strengths and Limitations



- **Balancing fidelity and feasibility with limited budget and personnel**
  - Who is the gold standard/ reference rater in each site?
- **Widely varied background of RAs**
  - From post-doc fellow/ junior faculty, MDs, RNs, and RAs with no clinical backgroun who just graduated from college.
    - Individual attention is absolutely necessary
    - Clinical background – not necessarily an advantage.
- **Rapid turn-over rate of RAs in some sites.**
  - High training burden.

Lessons learned

- Training and quality assurance for delirium assessment is an arduous, but absolutely necessary task.
- Rigorous training protocol and continuous quality assurance effort is necessary
  - A clinical trial is as good as the fidelity of its clinical outcome
- Need for more standardized assessment strategy before applying diagnostic instrument like CAM.
  - Especially for the non-clinical raters.

- WE ARE IN THE EARLY STAGE OF DEVELOPING THE FIELD – NEED TO LEARN FROM EACH OTHER

Gratitude

- Without their generous guidance and help, this presentation would not have been possible.
  - Focus Cognitive Ancillary Study
    - Anne Gruber-Baldini
    - Ed Marcantonio
  - STRIDE study
    - Frederick Sieber
  - Dexlirium Study
    - Jeff Silverstein
  - NIA for sponsoring the studies above