Advances in Geriatrics

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Enhancing Care for Veterans with Cognitive Impairment

Of the approximately 2.4 million veterans over the age of 65 who seek their medical care from the VA, about 7.3% have been diagnosed with dementia.[1] The prevalence of mild cognitive impairment (MCI) is about 4% in adults in their sixties[2] and rises to between 80% and 90% in the oldest-old (aged 85 years or older).[3] Over a lifetime, an average of 60% to 65% of individuals with MCI progress to dementia,[3] and the average annual conversion rate of MCI to dementia is about 14%.[4–6]

As a result of this prevalence and the aging of the population, the strain on veterans with dementia and their medical and nonmedical caregivers is growing and needs to be addressed in order to improve quality of care.[7] A major focus of the St. Louis Geriatric Research, Education and Clinical Center (St. Louis GRECC), located at the St. Louis VA Medical Center (VAMC), St. Louis, MO, has been enhancing care for the cognitively impaired veteran. A clear cognitive process is essential to a high quality of life. This column describes several noteworthy examples of the St. Louis GRECC's clinical and research efforts for addressing patient and clinician needs related to cognitive impairment.

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COGNITION SCREENING

Multiple studies have shown that both family members and physicians are slow to recognize dementia.[8,9] While the Mini-Mental State Examination (MMSE) has been the gold standard for screening for dementia,[10] recent enforcement of the test's copyright has created availability issues. In addition, the MMSE has been shown to perform poorly at identifying MCI.[11] For these reasons, we at the St. Louis GRECC attempted to develop a new screening test for dementia and MCI.

The test we developed was the Veterans Affairs/Saint Louis University Mental Status (VA SLUMS) examination (Figure). This test uses a modified clock drawing to increase detection of visual spatial problems, a common presenting feature in Alzheimer disease. It also has a five-word recall problem, as opposed to the three-word recall problem used in the MMSE. It includes an animal naming exercise that tests interference of previous words with the ability to continue finding new words. To evaluate executive function, we added a paragraph recall item that includes a test of the ability to recognize that a named city (Chicago) is in a state (Illinois) that is not named. The VA SLUMS examination is scored out of 30 points and takes about six and a half minutes to administer.

The VA SLUMS examination was validated against the MMSE and the criteria from the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*[12] in 702 veterans.[13] The study group had a mean age of 75.3 years, and two-thirds of the veterans had completed high school. They all were receiving their medical care through the St. Louis GRECC clinic. The VA SLUMS examination had a slightly better receiver operating characteristics (ROC) curve of sensitivity versus (1 – specificity) than did the MMSE for the detection of dementia. (An ROC curve plots true positives on the y-axis and false positives on the x-axis.) Additionally, the ROC curve for detection of MCI was better for the VA SLUMS examination than for the MMSE. Furthermore, since the VA SLUMS examination

The VHA's Geriatric Research, Education and Clinical Centers (GRECCs) are designed for the advancement and integration of research, education, and clinical achievements in geriatrics and gerontology throughout the VA health care system. Each GRECC focuses on particular aspects of the care of aging veterans and is at the forefront of geriatric research and clinical care. For more information on the GRECC program, visit the web site (http://www1.va.gov/grecc/). This column, which is contributed monthly by GRECC staff members, is coordinated and edited by Kenneth Shay, DDS, MS, director of geriatric programs for the VA Office of Geriatrics and Extended Care, VA Central Office, Washington, DC.

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DIAGNOSING DELIRIUM

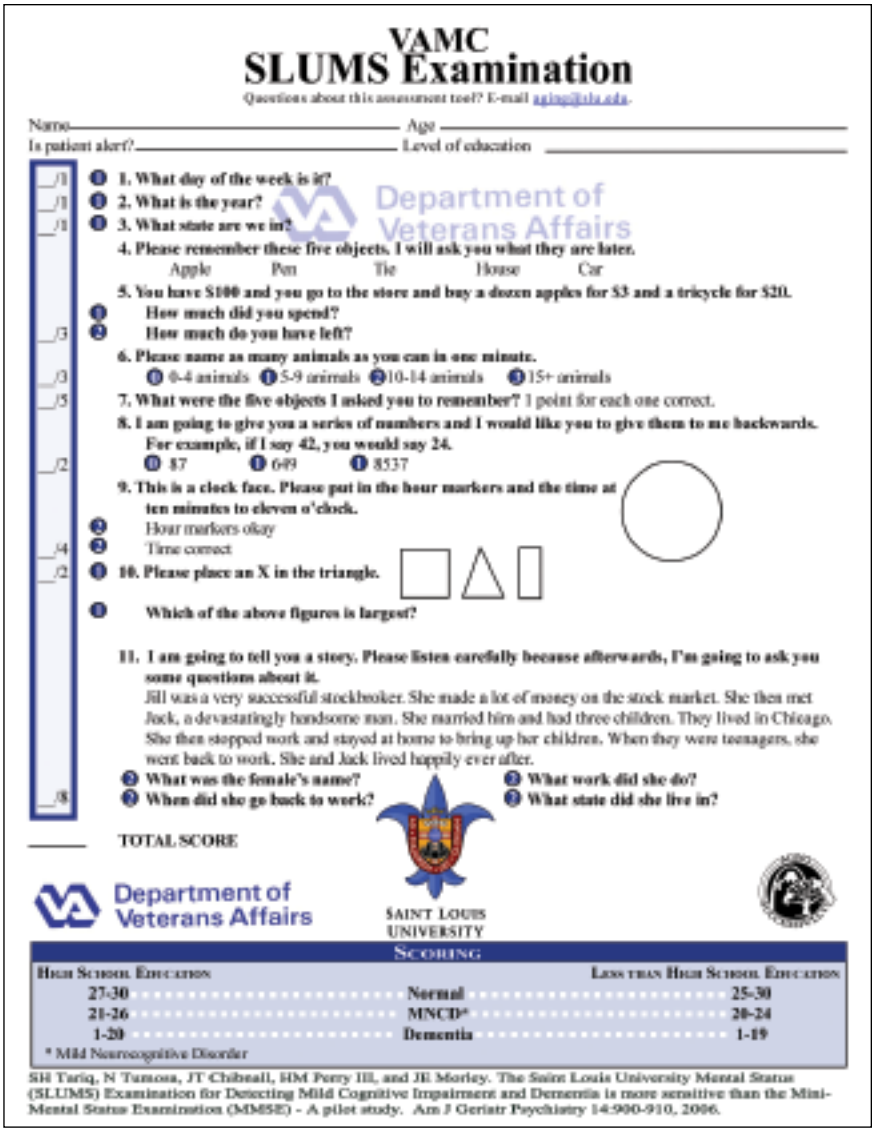
Delirium occurs in at least one third of older persons at the time of hospital admission, and it develops in another third during hospitalization.[14] Because delirium is such a serious and under-recognized problem, a VA working group—which includes Joseph Flaherty of the St. Louis GRECC—recently recommended that assessment of mental status should be considered the sixth vital sign.[14] In one study of patient care in the emergency department (ED), 83% of participants who were identified by the researchers as having delirium or "probable" delirium (using the Confusion Assessment Methodology administered immediately after the ED physician's examination) were not initially diagnosed as such by the ED physician.[15]

Because delirium often presents as fluctuating levels of attention, it is critical to get a history of cognitive status from the caregiver. Variable attention level can be diagnosed by asking the patient to lift his or her hand every time he or she hears a vowel in a list of vowels and consonants. Our studies also have shown that new onset of falling in an older person always should be considered to be an indicator of delirium until this has been ruled out.

From the educational perspective, we have developed the "DELIRIUM(S)" mnemonic to help recognize the multiple causes of delirium (Table).

INPATIENT MANAGEMENT OF DELIRIUM

In the hospital, patients with delirium have higher mortality, have a greater length of stay, and are more likely to have functional deterioration



VAMC
SLUMS Examination

Questions about this assessment tool? E-mail aging@slu.edu.

Name_____ Age_____
Is patient alert?_____ Level of education_____

__/1 1. What day of the week is it?
__/1 2. What is the year?
__/1 3. What state are we in?

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4. Please remember these five objects. I will ask you what they are later.
Apple Pen Tie House Car

5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20.
How much did you spend?
__/3 How much do you have left?

6. Please name as many animals as you can in one minute.
__/3 0-4 animals 5-9 animals 10-14 animals 15+ animals

__/5 7. What were the five objects I asked you to remember? 1 point for each one correct.

8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.
__/2 87 649 8537

9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
Hour markers okay
__/4 Time correct

__/2 10. Please place an X in the triangle.

Which of the above figures is largest?

11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.
Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.
What was the female's name?
__/8 When did she go back to work?
What work did she do?
What state did she live in?

_____ TOTAL SCORE

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Scoring		
High School Education		Less than High School Education
27-30	Normal	25-30
21-26	MNCD*	20-24
1-20	Dementia	1-19

* Mild Neurocognitive Disorder

Siil Tariq, N Tumosa, JT Chibnall, HM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for Detecting Mild Cognitive Impairment and Dementia is more sensitive than the Mini-Mental Status Examination (MMSE) - A pilot study. Am J Geriatr Psychiatry 14:900-910, 2006.

Figure. The Veterans Affairs/Saint Louis University Mental Status (VA SLUMS) examination, a screening test for mild cognitive impairment and dementia, developed by researchers from the St. Louis Geriatric Research, Education and Clinical Center and St. Louis University School of Medicine.

than those without delirium.[16] Yet few models for managing delirium have been developed in hospitals, despite the obvious financial incentive for their creation.

In response to this need, we have created a "delirium room" that provides a new model of care for hospitalized patients with delirium.[17] This delirium room is a four-bed unit, located on a medical floor of the university hospital affiliated with the St. Louis GRECC, that provides around-the-clock intensive nursing care. The unit is staffed by a full-time registered nurse or licensed practical nurse. It is well lit in order to decrease the potential for the sighting of illusory objects. The use of physical restraints is forbidden—including Foley catheters, which are one-point restraints. The floor staff holds daily team meetings,

and physicians are required to attend the meetings on at least five days of the week. On the days that they are not able to attend the team meetings, physicians are made aware of the presence of patients in the delirium room. The multifactoral nature of delirium is stressed constantly. Because antipsychotics can worsen delirium, the use these drugs is deemphasized and is reserved for instances of clear paranoid or psychotic behavior. We also avoid the use of sedatives in the delirium room; when it is necessary to calm a patient, we use a low dose of lorazepam. Bed rest is discouraged. All patients receive comprehensive geriatric care.

In a retrospective study, we demonstrated that the use of the delirium room resulted in patients with delirium having the same length of hospital stay, the same in-hospital mortality rate, and slightly lower costs than age- and diseased-matched patients without delirium.[17] Based on these findings, we strongly recommend the use of a delirium room as a cost-effective method for managing delirium in the inpatient setting. Clearly, a controlled research study involving delirium rooms at several GRECCs would be appropriate to determine whether all VA medical centers would benefit from the adoption of the delirium room model.

DISEASE MODIFYING DRUGS FOR ALZHEIMER DISEASE

The drugs available to manage Alzheimer disease—specifically, the cholinesterase inhibitors and memantine—have been shown to produce a mild statistical improvement in cognition. These drugs, however, are not considered to have a clinically significant effect.[18,19]

These disappointing results have led researchers at the St. Louis GRECC to embark on a search for disease modifying drugs. Our group has shown that antibodies to amyloid-beta protein can improve memory and cholinergic function in mice when injected into the brain's ventricles.[20,21] In addition, antibodies that cross the blood-brain barrier and show central effects can be administered peripherally.[22] The first attempt at a trial of immunization of humans against amyloid-beta protein, however, was interrupted when 6% of the participants developed meningoencephalitis.[23] While there was some decrease in amyloid plaques, no clear memory effects could be demonstrated.[23]

Also at the St. Louis GRECC, gamma-secretase modulators and inhibitors are being developed. These drugs modulate the enzymes responsible for the production of amyloid-beta-42 and, as such, selectively lower some forms of amyloid-beta. While these drugs clear plaques in animals, the human studies have failed to produce a clinically significant effect. A number of amyloid aggregation inhibitors have been developed. Tramiprosate binds to soluble amyloid-beta protein, preventing plaque development. Clinical trials are presently ongoing.

Our research group at the St. Louis GRECC has taken a novel approach to the development of a disease modifying drug. Dr. Vijaya Kumar developed a number of antisenses to the messenger RNA for amyloid precursor protein. (Antisense mRNA is the noncoding strand complementary to the coding sequence of mRNA. Introducing a transgene coding for antisense mRNA is a strategy used to block expression of a gene of interest.) Originally, we showed that these antisenses inhibit amyloid-beta protein in cell culture.[24] We then demonstrated that, when administered intracerebroventricularly in the SAMP8 mouse, an animal model of amyloid-beta protein overproduction,[25] we could enhance memory.[26] Subsequently, we found that antisense to amyloid precursor protein reversed oxidative damage in the brain and reversed the delayed amyloid-beta clearance from the brain in mice models of Alzheimer disease.[27,28]

We then demonstrated that the antisense could cross the blood-brain barrier and could reverse memory deficits when given peripherally.[29] The antisense also was shown to enter cells. Finally, we showed it could be administered intranasally. Based on these animal studies, we are now preparing to begin preliminary human studies.

Table. DELIRIUM(S): A mnemonic device for the possible causes of delirium[a]

- **D**rugs
- **E**yes, ears
- **L**ow O_2 states (MI,[b] stroke, PE[c])
- **I**nfection
- **R**etention (of urine or stool)
- **I**ctal
- **U**nderhydration/undernutrition
- **M**etabolic
- **(S)**ubdural

[a]It's important to remember that delirium usually has more than one cause. [b]MI = myocardial infarction. [c]PE = pulmonary embolism.

CONCLUSION

The 21st century will see incredible advances in our understanding of the brain. The St. Louis GRECC researchers are playing a leadership role in discovering mechanisms of brain function. Through better understanding of brain function, we hope to develop approaches to improving the care of older persons with delirium and dementia. It is hoped that this improved care will result in a better quality of life for those with cognitive diseases.

Author disclosures

Dr. Tumosa reports no actual or potential conflicts of interest with regard to this column. Dr. Morley reports that he is a founding director of EDUNN Biotechnology Inc., which is involved in developing antisense to amyloid precursor protein for treatment of Alzheimer disease. He holds patents with EDUNN; receives grant/research support from Ascend, Baxter, and Numico; is on the speaker's bureaus of Merck & Company, Novartis, Indevus, Orthobiotec, GTx, Amgen, Novartis Nutritional, and Mattern Pharmaceuticals; is a consultant for Novartis, Mattern Pharmaceuticals, Amgen, EDUNN, Indevus, Abbott, GlaxoSmithKline, Cytokinetics, Ligand, and Baxter; and owns stocks in Mattern Pharmaceuticals and EDUNN.

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