Mild cognitive impairment (MCI), dementia, and depression are common in elderly patients. Three new studies focus on the link between lower levels of serotonin transporters in the brain and MCI; a noninvasive method to distinguish Alzheimer disease (AD) from frontotemporal dementia; and the effectiveness of ketamine for depression in older adults.[1-3] Scroll through the slides for the latest findings and take-home messages.
Study 1. Lower Levels of Brain Serotonin Linked to Cognitive Decline

Persons With MCI Have Lower Brain Levels of Serotonin Transporters Than Healthy Controls: Previous studies have shown that those with AD and severe cognitive decline have severe loss of serotonin neurons. A new study included 56 participants (mean age, 66 years), 28 with MCI and 28 healthy matched controls.

The participants underwent MRI and PET scans to measure brain structures and levels of a serotonin transporter. Those with MCI had up to 38% less serotonin transporter detected in their brains compared with controls, and this finding correlated with greater deficits in auditory-verbal and visual-spatial memory in those with MCI, but not in controls.[1]
Clinical Implications for Study 1: The results suggest that prevention of the loss of serotonin or introduction of a substitute neurotransmitter could slow or stop the progression of AD and perhaps other dementias.

“Now that we have more evidence that serotonin is a chemical that appears affected early in cognitive decline, we suspect that increasing serotonin function in the brain could prevent memory loss from getting worse and slow disease progression,” said lead author Gwenn Smith, PhD, of the Johns Hopkins University School of Medicine in Baltimore, MD. Dr. Smith suggested that PET imaging of serotonin could be a marker to detect progression of disease.
Transcranial Magnetic Stimulation (TMS) Can Reliably Differentiate AD From Frontotemporal Dementia:

Frontotemporal dementia, which comprises up to 15% of dementia cases, is often initially misdiagnosed as AD or Parkinson disease because of its wide range of symptoms. A study designed to distinguish AD from frontotemporal dementia included 175 participants: 79 with AD, 64 with frontotemporal dementia, and 32 healthy controls.

Using pair-pulsed TMS, AD patients were characterized by a specific impairment of short-latency afferent inhibition, and those with frontotemporal dementia showed a dysfunction of short-interval intracortical inhibition and facilitation intracortical circuits. TMS differentiated frontotemporal dementia from AD with a sensitivity of 91.8% and a specificity of 88.6%, AD from healthy controls with a sensitivity of 84.8% and a specificity of 90.6%, and frontotemporal dementia from healthy controls with a sensitivity of 90.2% and a specificity of 78.1%.[2] These results were confirmed in patients with mild disease.
Clinical Implications for Study 2: “Making the correct diagnosis can be difficult,” said senior author Barbara Borroni, MD, of the University of Brescia in Brescia, Italy. “Current methods can be expensive brain scans or invasive lumbar punctures involving a needle inserted in the spine, so it’s exciting that we may be able to make the diagnosis quickly and easily with this noninvasive procedure. Doctors might soon be able to quickly and easily diagnose frontotemporal dementia with this non-invasive procedure. This disease unfortunately can’t be cured, but it can be managed, especially if it is caught early.”
Study 3. KETAMINE EFFECTIVELY TREATS DEPRESSED ELDERLY PATIENTS

3. Preliminary Evidence Suggests Ketamine Is a Safe and Effective Treatment for Depression in Elderly Patients: A double-blind, controlled, multiple-crossover study included 16 participants (age 60 or older) with treatment-resistant depression who relapsed after remission. They received up to 5 subcutaneous doses of ketamine in separate sessions 1 or more weeks apart, with one active control (midazolam) randomly inserted during a randomized controlled trial (RCT) phase. The participants also received 12 ketamine treatments in an open-label phase.

Seven of the 14 patients who completed the RCT phase remitted with ketamine treatment, and the drug was well tolerated. Repeated treatments resulted in higher likelihood of remission or longer time to relapse.
Clinical Implications for Study 3: The results indicate a dose-titration method of ketamine may be particularly useful for older patients. “These findings take us a big step forward as we begin to fully understand the potential and limitations of ketamine’s antidepressant qualities,” said lead author Colleen Loo, MD, School of Psychiatry, University of New South Wales, Sydney, New South Wales, Australia. “Not only was ketamine well-tolerated by participants, with none experiencing severe or problematic side effects, but giving the treatment by a simple subcutaneous injection was also shown to be an acceptable method for administering the drug in a safe and effective way.” Future studies with greater sample sizes are needed to formally assess ketamine’s side effects, such as its impact on liver function, she said.
REFERENCES

