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Stephanie Collier, MD, MPH
Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Diagnostic Challenges in Older Adults

Learning Objectives

After reading these articles, you should be able to:

1. Differentiate between and treat the 3 Ds of geriatric psychiatry.
2. Describe the course of personality disorders in older adults.
3. Identify circumstances in which neuroimaging is indicated in the evaluation of older adults.
4. Summarize some of the findings in the literature regarding psychiatric treatment for older adults.

The 3 Ds of Geriatric Psychiatry: Depression, Dementia, and Delirium

Rachel Meyen, MD. Outpatient geriatric psychiatrist, General Mental Health Clinic, Sacramento VA Medical Center, Mather, CA.

Dr. Meyen, author of this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

Both common yet elusive, symptoms of depression, dementia, and delirium may overlap in older adults, proving a diagnostic challenge. Even more confounding, these three disorders—the 3 Ds—frequently present simultaneously (Downing LJ et al, *Curr Psychiatry Rep* 2013;15(6):365). This article will review key features to help distinguish between these disorders and provide tips on their management.

Highlights From This Issue

Feature article
In differentiating between depression, dementia, and delirium, the time course of symptoms may help you the most.

Feature Q&A
As first-episode mania in late life is very uncommon, think about dementia, neurological illness, substances, or delirium first.

Q&A on page 8
Dr. Olusola Alade Ajilore walks us through scenarios to help determine when imaging studies are appropriate to differentiate between dementias.

Depression

Older adults may experience "depression without sadness"—this may manifest as anhedonia or somatic symptoms, fatigue, apathy, and general malaise. They

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Q&A With the Expert

Personality Changes Later in Life: Diagnostic and Treatment Considerations
Rajesh R. Tampi, MD

Professor and chairman, Department of Psychiatry, Bhatia Family Endowed Chair in Psychiatry, Creighton University School of Medicine. Catholic Health Initiatives (CHI) Behavioral Health Services, Omaha, NE.

Dr. Tampi, expert for this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

CGPR: What is the course of personality disorders as people age?

Dr. Tampi: Personality usually doesn't change much. People with borderline personality disorder (BPD), for example, don't usually experience significant changes once they reach middle age. Experiences over a person's lifespan may teach them skills that blunt their sharp edges, but the core features of maladaptive behavior patterns remain. Although people with BPD often show high rates of remission and low rates of relapse, they continue to experience severe and persistent impairment in social functioning (Gunderson JG et al, *Arch Gen Psychiatry* 2011;68(8):827–837). If you see a major change in personality as a person ages, you'd suspect a primary psychiatric illness, substance use, major neurocognitive disorders, or delirium.

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Expert Interview – Personality Changes Later in Life: Diagnostic and Treatment Considerations

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CGPR: Can you provide an example of a change in personality due to another condition?

Dr. Tampi: I recently saw a 77-year-old woman who presented with language abnormalities and personality changes—her husband now walks on eggshells around her. On the initial Montreal Cognitive Assessment (MoCA), she scored 30 out of 30, but her husband was sure something was going on. Since the initial evaluation, the patient has continued to decline both cognitively and functionally. Her last MoCA score was 23/30. I diagnosed her with major neurocognitive disorder, possibly due to Alzheimer's disease (AD), although her language and personality changes would also be consistent with frontotemporal dementia (FTD). I thought the diagnosis of AD would be more appropriate given her senile onset, associated memory decline, and lack of associated executive dysfunction.

CGPR: In your experience, do clinicians often miss personality disorders in older adults?

Dr. Tampi: Yes. As with any other disorder, we miss what we're not looking for. Clinicians may not realize that patients have a personality disorder if it hasn't been previously diagnosed, so they may wonder why an 80-year-old is presenting with symptoms of a personality disorder. It's a longitudinal diagnosis, so it's difficult to make; the patterns of maladaptive behaviors must be enduring. You will need collateral when evaluating personality changes.

CGPR: As people with personality disorders age, do their self-harming behaviors increase in frequency?

Dr. Tampi: There is a smaller role for cluster B personality disorders in late-life suicide compared to suicide in younger adults, although there is a possible role for cluster C disorders such as obsessive-compulsive personality disorder (OCPD) (Szücs A et al, *Front Psychiatry* 2018;9:128). Deliberate self-harm declines with age. Other maladaptive patterns of behavior, such as excessive drinking or gambling, also decline with age (Welte JW et al, *J Gambl Stud* 2011;27(1):49–61).

CGPR: How do you document suspicion of a personality disorder, especially since patients have access to their own records?

Dr. Tampi: I say to every patient: "It's your health and your chart. You own the chart; I don't. I just document in it." I tell the patient that I will not say or do anything that they don't know about. When I suspect a personality disorder, I say something like: "Has anybody discussed that the difficulties you have in life could be because of personality issues?" I don't make it a negative thing by calling it a disorder. Sometimes patients respond: "People have said that I may have BPD." If they do, my next questions are something like: "What is your understanding about it? What would you like to do about it? Would you like therapy?" Many times, patients are then agreeable.

CGPR: Can you give me an example of this documentation strategy?

Dr. Tampi: If I have a discussion with a patient whom I suspect has narcissistic personality disorder and poor insight, I would document that we discussed the possibility of narcissistic personality issues and that the patient disagreed with the suggestion.

CGPR: What's on your differential diagnosis in an older adult with new-onset mania or hypomania?

Dr. Tampi: I think about disorders that are secondary to either a medical condition or substance use. I also think about bipolar disorder, schizophrenia, or schizoaffective disorder.

CGPR: How do you narrow down your differential?

Dr. Tampi: The diagnosis is made through a good history, a thorough physical examination, appropriate laboratory testing, screening tools, and neuropsychological testing if the diagnosis remains unclear. I tell my patients that we may not get it right the first time around because we are gathering information; we start by sorting out what conditions are most likely and then work down the ladder. I follow a standardized process for all of my patients to minimize my chances of missing something. For the history, I assess whether my patient has experienced a previous episode of mood instability. I then clarify whether they are experiencing mood instability alone or in combination with other features. I also rule out underlying medical causes, such as hypothyroidism. I review their medications, paying special attention to stimulants, but I also ask about drugs of abuse. Finally, I assess whether my patient experiences cognitive issues, as many neurodegenerative disorders can have mood instability as their first presenting symptom.

CGPR: When an older adult experiences their first episode of mania or hypomania, what are the chances that it's due to new-onset bipolar disorder versus something else?

Dr. Tampi: First onset of bipolar is uncommon in late life. The typical age of onset is usually in the late teens/early adulthood, although a small number of patients develop classic manic symptoms in late life. The one-year prevalence of bipolar disorder is around 0.4% in adults 65 years and older (Blanco C et al, *J Psychiatric Res* 2017;84:310–317).

CGPR: Those numbers are extremely low.

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Dr. Tampi: For classic bipolar disorder, onset in late life is very uncommon. I can think of only a handful of my patients who presented with their first episode in older age. That is why I think about delirium, stroke, head injuries, tumors, or medication effects (such as stimulants or steroids) in older adults with mood instability.

CGPR: What is the relationship between FTD and bipolar?

Dr. Tampi: Patients with FTD may present with similar symptoms, including mood instability, apathy, and executive dysfunction. But you may not see progression until years later, and when you look back on it, you will say, "We should have thought about it." When I see a patient with classic manic or hypomanic symptoms, the first thing that comes to my mind is whether this could be the behavioral variant of FTD. Following the patient will point you to FTD if there is progression in symptoms over time.

CGPR: What points you toward FTD when following a patient over time?

Dr. Tampi: Initially, your data will not help you much. Neuroimaging studies will be normal early on. When you strongly suspect early-onset FTD, a positron emission tomography (PET) scan may be helpful because it shows hypofrontality (decreased blood flow in the prefrontal cortex). To date, I have only sent one patient for a PET scan: a younger patient who had symptoms that seemed to be more consistent with FTD than AD. The classic phenotype of a person with FTD is early onset, and 25%–40% of these individuals have a family history, which may contain additional clues to warrant further evaluation. Genetic testing can also be helpful.

"I can think of only a handful of my patients who presented with their first episode of bipolar disorder in older age. That is why I think about delirium, stroke, head injuries, tumors, or medication effects in older adults with mood instability."

Rajesh R. Tampi, MD

CGPR: What do you think about neuropsychological testing to identify FTD in its early stages?

Dr. Tampi: I have had very good results in early stages. Neuropsychologists will be able to distinguish a psychiatric illness from a neurodegenerative illness. They can differentiate pseudodementia of depression from a primary dementia process. Testing can clarify the etiology based on the pattern of deficits. In early stages, people with FTD have frontal executive dysfunction and abnormalities in social cognition. You may not see it initially, but as the illness progresses, it becomes clear.

CGPR: How do you approach the management of disinhibition, as a result of vascular or neurodegenerative changes, in a nonpharmacological way?

Dr. Tampi: It depends on the etiology. In the case of a neurocognitive disorder, I work with the patient and family members on behavioral management techniques, such as redirection. I try to have them minimize risk-taking behaviors (eg, by taking away car keys). Therapy is challenging, as patients with disinhibition may not always have insight into their behaviors.

CGPR: And when it's not enough, what are your next steps?

Dr. Tampi: Medications. There is little evidence to guide you in the management of behavioral issues. Antidepressants are helpful because they decrease obsessive behaviors and impulsivity in people with personality disorders. In patients with mood instability, you can use anticonvulsants and antipsychotics. For people with FTD, stimulants can be very beneficial (Young JJ et al, *Ther Adv Psychopharmacol* 2018;8(1):33–48). You might think that a stimulant would make things worse, but increasing norepinephrine and dopamine decreases hypofrontality and can thus help with impulse control, reasoning, etc. Stimulants help with disinhibition—they improve a person's focus, including attention paid toward social cues. They also seem to help with apathy and risk-taking behaviors in this population.

CGPR: When considering a neurocognitive disorder as an explanation of the patient's behavioral changes, what do you focus on in the neurological exam?

Dr. Tampi: In a standard neurological examination, I look for findings as a result of vascular changes, such as hemiparesis, weakness, or incoordination. However, unless the neurovascular burden is high, patients may not have any neurological signs. If I'm in doubt, I will co-manage the patient with a neurologist. This may occur in a patient with FTD and Parkinsonism, for example.

CGPR: What else do you look for in the physical and neurological exam?

Dr. Tampi: The examination starts in the waiting room. I assess the patient's gait, tone, and arm swing. I look for tremors and gaze abnormalities. And then I look for changes in speech—assessing motor functioning, repetition, and comprehension.

CGPR: Which screening tools do you use beyond the MoCA when thinking about personality changes in late life?

Dr. Tampi: The MoCA picks up on mild neurocognitive disorders and subtle executive dysfunction. I don't do any separate personality assessments. I may ask a neuropsychologist when the diagnosis is in doubt, and they can use the Minnesota Multiphasic Personality Inventory (MMPI) and additional personality assessments. Personality changes secondary to a neurocognitive disorder should not be labeled as a personality disorder. When I suspect personality changes secondary to FTD, I tell the family that I will defer the diagnosis until I have more data. I would not want to mislabel a personality disorder, although I also recognize that limiting the differential can be problematic.

CGPR: How should clinicians proceed if they don't have access to a neuropsychologist, or if they have limited access to imaging?

Dr. Tampi: When clinicians do not have access to specialized imaging or neuropsychologists, I would recommend co-managing with a neurologist. Clinicians can also discuss the "provisional diagnosis." Labeling is a big issue in

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Expert Interview – Personality Changes Later in Life: Diagnostic and Treatment Considerations

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geriatrics, with very real implications for financial and legal independence, driving, and decision-making. An incorrect diagnosis can change the way patients perceive themselves and their difficulties, and this is especially true with personality changes.

CGPR: So, when you speak with families, you speak about provisional diagnoses?

Dr. Tampi: Correct. I say to every patient, "You drive the agenda, not me." My goal is to help them improve their quality of life. A provisional diagnosis may change as you obtain more information from the chart, previous clinicians, or family members. I treat what is right in front of me and continue to work up the diagnosis and revise as needed.

CGPR: Thank you for your time, Dr. Tampi.

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The 3 Ds of Geriatric Psychiatry: Depression, Dementia, and Delirium

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are also at higher risk of experiencing psychotic symptoms of depression, with delusions present in up to 45% of older adults admitted to hospitals due to depression (Tampi RR et al, *Ther Adv Psychopharmacol* 2019;9:2045125319882798). Most commonly, psychotic symptoms manifest as auditory hallucinations (often derogatory comments), paranoia, or nihilistic delusions. When patients experience visual hallucinations, I think instead about delirium, Lewy body dementia, ophthalmological conditions, or brain injury. Patients with an increased vascular burden in the brain and a history of stroke are at a higher risk for developing depression. Depression is also commonly seen as a non-motoric symptom of Parkinson's disease.

Apathy—a lack of motivation or interest in the absence of a subjectively low mood—may mimic depression and is a common early symptom of dementia.

Assessment

In addition to checking labs to rule out reversible causes of depression (see "Differentiating Among the 3 Ds" table on page 5), I screen for sleep apnea using the STOP-BANG sleep apnea questionnaire (www.stopbang.ca/about/contactus.php).

The Geriatric Depression Scale (GDS) Short Form is a helpful screener for depression in older adults (www.tinyurl.com/2w944rp4). In patients with no prior history of depressive symptoms, I always ask about subjective cognitive concerns, as late-onset depression can herald a budding neurocognitive disorder. In all patients with depression, I pay attention to suicide risk factors, as older men have the highest risk for completed suicide (Conwell Y et al, *Psychiatr Clin North Am* 2011;34(2):451–468). *(Editor's note: We will cover suicide risk in older adults in more detail in an upcoming issue of the* Carlat Geriatric Psychiatry Report.*)*

Management

Selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and mirtazapine are popular first choices. I keep the following saying in mind: "Start low, go slow, but go all the way," as medications are often underdosed in older adults. As an example, I may start mirtazapine at 7.5 mg at bedtime (or 3.25 mg in frailer patients), increasing in 7.5 mg intervals to a target range of 15–30 mg at bedtime.

Individual psychotherapy interventions, including cognitive behavioral therapy (CBT), problem solving therapy (PST), and interpersonal therapy (IPT), are considered evidence-based practices for late-life depression. Additionally, group therapy can significantly improve symptoms of late-life depression. Consider daily bright light therapy, which may also be effective in non-seasonal late-life depression, or transcranial magnetic stimulation (TMS), although TMS is less effective than electroconvulsive therapy (ECT). For severe or treatment-refractory depression, ECT remains the most efficacious treatment and is well tolerated in the elderly.

Dementia

Dementia is a decline in cognitive function that impacts activities of daily living (ADLs). The most common dementia is Alzheimer's disease (AD), characterized by the insidious progression of symptoms such as short-term memory loss and word-finding difficulties over the years. When cognition changes over days or weeks, I think of depression or delirium.

Assessment

I screen cognition with one of the following:

- Mini Mental Status Exam (MMSE; www.tinyurl.com/mr2t7xv2)
- Montreal Cognitive Assessment (MoCA; www.tinyurl.com/2p983taz)
- St. Louis University Mental Status Examination (SLUMS; www.tinyurl.com/2p9by8k7)

In addition to the standard dementia labs, think about brain imaging (either head CT or brain MRI), especially if you suspect an atypical course of dementia, see focal neurological signs, or suspect a large vascular burden as a contributor to depression.

Management

I try to optimize nonpharmacological treatments first. These include problem-solving therapies, psychosocial interventions, and caregiver support. Activity scheduling and enhancing daytime structure may improve apathy associated with dementia.

Although cognitive enhancers do not reverse dementia, they may alleviate some of the symptoms. Cholinesterase inhibitors are used for mild, moderate, or severe AD, while memantine is reserved for moderate to severe cases. Melatonin can be helpful for maintaining a normal sleep-wake cycle in patients with dementia.

Delirium

Delirium is an acute confusional state due to a medical illness or its treatment. It develops quickly, usually over the course of hours or days, and fluctuates in severity. Delirium is considered the lupus of psychiatry—it can masquerade as many other psychiatric illnesses. Patients with hypoactive delirium may appear "depressed," those with hyperactive delirium may appear "manic" or "psychotic," and those with confusion may appear "intoxicated" or "cognitively impaired." In patients with

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delirium, acute changes in environment can lead to rapid behavioral decompensation.

The pathophysiology of delirium involves the dysregulation of multiple neurotransmitter systems, disrupting network connectivity in the brain. Although the community prevalence of delirium is low, it occurs in 10%–30% of hospitalized elderly patients (Gagliardi JP, *Virtual Mentor* 2008;10(6):383–388).

Assessment

In an older adult with delirium, our priority is to rule out life-threatening causes. I start with a review of a patient's vital signs and nursing notes to appreciate the time course of the patient's altered mental status. I review all medications, paying close attention to those known to cause delirium, such as benzodiazepines, anticholinergics, and opioids. I try to rule out infections (UTIs and pneumonias being the most common), electrolyte abnormalities, alcohol or benzodiazepine withdrawal, and other medical illnesses. I also evaluate whether the patient is experiencing pain, hunger, constipation, or changes in sleep patterns. *(Editor's note: For more on assessing and treating delirium in older adults, see article in this issue.)*

After thinking through reversible medical causes, I move on to the psychiatric differential. Highest on my differential is dementia—I assume every older adult with delirium has an underlying dementia until proven otherwise. I also consider apathy, depression, and catatonia. To quickly and accurately screen for delirium in older adults, I recommend the 3-D Confusion Assessment Method (CAM) screening tool (www.tinyurl.com/2v295c2w). This screener includes four features that help distinguish delirium from other types of cognitive impairment.

When differentiating between depression, dementia, and delirium, timing is everything (see table). Worsening cognition over days and weeks, in addition to a fluctuating course, is most consistent with delirium. Although dementia progresses over months to years, it can certainly underlie delirium. Delirium (especially hypoactive delirium) can also mimic depression. To disentangle these conditions, testing attention is key—*if attention is intact, the patient is not delirious*. The fastest way to assess attention is to ask the patient to recite the months of the year (or the days of the week) backwards. If the patient is delirious, remember that no other psychiatric diagnosis can be made in its presence, as delirium holds a place of diagnostic privilege.

Differentiating Among the 3 Ds

	Depression	Dementia	Delirium
Symptoms	• Apathy • Anhedonia • Depressed mood • Poor energy • Somatic concerns, fatigue, malaise	• Irreversible cognitive changes that interfere with ADLs	• Acute waxing and waning sensorium • Inattention
Time Course	• At least two weeks	• Months to years	• Days to weeks
Screening	• Geriatric Depression Scale	• MoCA • MMSE • SLUMS	• CAM
Recommended Labs	• CBC • Comprehensive metabolic panel (CMP) • Folate • RPR • TSH • Vit B_{12}	• CBC • CMP • Folate • RPR • TSH • Vit B_{12} • Vit D	• Blood alcohol level • CBC • CMP • Folate • TSH • Urinalysis • Urine drug screen • Vitamin B_{12}
Neuroimaging	• Brain MRI if concern for vascular depression	• Brain MRI	• CT head if focal neurological symptoms
Common Pharmacologic Treatment	• Antidepressants	• Cholinesterase inhibitors • Melatonin or ramelteon • Memantine	• Antipsychotics for agitation • Melatonin or ramelteon
Nonpharmacologic Treatment	• Cognitive behavioral therapy • ECT • Interpersonal therapy • Problem solving therapy • TMS	• Caregiver support • Problem-solving therapy • Psychosocial interventions	• Frequent reorientation • Maintaining sleep-wake cycle

Management

Nonpharmacological interventions have the best evidence and can reduce the incidence of delirium by up to 40% (Inouye SK et al, *Lancet* 2014;383(9920):911–922). I try to keep patients with delirium awake and alert during the day by engaging in activities and conversation, as well as keeping them out of bed if possible. I recommend that windows be kept open to sunlight during the day and that rooms remain dark and relatively undisturbed for sleeping at night. As delirium affects the sleep-wake cycle, wander guards, door alarms, and GPS chips can help ensure patients' safety in case they wander at night.

I avoid antipsychotics unless physical aggression or psychosis pose a danger to the patient or others. I carefully weigh the benefits of decreasing agitation with the risks of antipsychotics—especially in patients with comorbid dementia, given the FDA's black box warning of an increased risk of death in individuals with neurocognitive disorders. For physical aggression unresponsive to nonpharmacological strategies, I start with quetiapine 12.5–25 mg or olanzapine 2.5–5 mg either at bedtime or twice daily as needed. I may also consider haloperidol 0.5–1 mg every two to four hours, which has the advantage of availability in PO, IM, and IV formulations. Although antipsychotics can decrease agitation, they have no effect on delirium severity, resolution of other delirium symptoms, or

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Assessing and Treating Delirium in Older Adults

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Delirium is one of the most perplexing psychiatric findings in older adults. It is defined as a disturbance of attention and a change in cognition. Delirium can be a cause of altered mental status (AMS), which is a general term defined as a change in mental functioning affecting cognition, consciousness (from slight confusion to coma), or both. Delirium affects both cognition and consciousness, whereas dementia affects cognition but preserves consciousness. This article will shed some light on assessing and working up delirium in older adults.

Time frame

Start by establishing the period over which the symptoms developed. Family and friends are often helpful here. Knowing the episode's duration can help you narrow down its cause and choose your next course of action.

Delirium occurs over minutes to days. The more acute and rapid the change, the more often it's life threatening. Subacute AMS happens over weeks to months, while chronic AMS takes place over months to years (Smith AT and Han JH, *Semin Neurol* 2019;39:5–19). See "Selected Causes of Altered Mental Status" table for potential causes of AMS as well as other important considerations.

Predisposing and precipitating risk factors for delirium

Delirium is a relatively common cause of AMS. It is always caused by underlying medical conditions or medications/substances. Typically, there's more than one cause. It's important to identify the cause(s) of delirium because correcting the underlying disturbance is the primary treatment. While mental health clinicians may not be responsible for treating core medical illnesses, we often must be the ones to ensure that a complete workup has been done. It's also within our role to review the medication list and work with other clinicians to taper off problematic drugs.

It's important to pay attention to risk factors, because reducing them can help prevent or shorten the course of delirium. *Predisposing* risk factors increase the risk of delirium, while *precipitating* risk factors trigger delirium. Precipitating risk factors are further separated into acute insults, environmental exposures, and delirium-inducing medications. See "Contributing Causes of Delirium" table on page 6.

Physical/neurological examination—high-yield pearls

A focused physical exam can provide valuable information about the origin of a patient's AMS.

Head

Look for signs of trauma, which could suggest an intracranial hemorrhage. Battle's sign (bruising behind the ear) indicates a possible skull base fracture.

Eyes

1. Pinpoint pupils (1–2 mm) are a hallmark of opioid toxicity. Dilated pupils are seen with anticholinergic toxicity.
2. Bulging eyes can be a sign of hyperthyroidism, infection, or trauma.
3. Paralysis of the outward eye movements is an indicator of either Wernicke's encephalopathy, caused by thiamine deficiency, or increased intracranial pressure.
4. Yellowed eyes occur in liver failure and are due to increased bilirubin.

Neck

Neck stiffness, headache, and photophobia point toward meningitis.

Neurological

1. Disorientation is seen in delirium.
2. Impaired attention is the hallmark feature of delirium. You can rapidly assess attention by asking the following two questions:
   - "Please tell me the day of the week."
   - "Please tell me the months of the year backwards starting with December."

   In a study of 201 participants (mean age 84 years, 62% female), if both answers were incorrect, this screen had 93% sensitivity and 64% specificity in picking up AMS (Fick DM et al, *J Hosp Med* 2015; 10(10):645–650).

Selected Causes of Altered Mental Status

	Acute	Subacute	Chronic
Medical	• Hypertensive emergency • Infections • Medications • Metabolic abnormalities • Toxins	• Autoimmune diseases • Endocrine dysfunction • Infections • Malignancy • Vitamin deficiencies	• Autoimmune diseases • Endocrine dysfunction • Infections • Obstructive sleep apnea • Renal/liver failure • Vitamin deficiencies
Neurological	• Brain hemorrhage • Migraine • Seizure • Stroke • Traumatic brain injury	• Prion disease • Subdural hemorrhage	• Dementia • Normal pressure hydrocephalus • Subdural hemorrhage
Psychiatric	• Alcohol or substance intoxication/withdrawal • Catatonia • Conversion disorder • Mania • Non-epileptiform seizures • Panic attacks • Psychosis	• Conversion disorder • Depression • Psychotic disorder	• Depression • Psychotic disorder

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Contributing Causes of Delirium			
Predisposing Factors	**Acute Insults**	**Environmental Exposures**	**Medications**
• Advanced age • Deconditioning • Dementia • Hearing/visual impairment • Kidney or liver disease • Malnutrition • Polypharmacy • Substance use	• Dehydration • Fracture • Hypoxia • Infection • Malnutrition • Metabolic abnormalities • Pain • Severe illness • Surgery • Trauma • Urinary or stool retention	• Intensive care unit • Restraints • Sleep deprivation	• Anticholinergics • Benzodiazepines • Corticosteroids • Dopamine agonists • Narcotics including meperidine • Sedative/hypnotics • Valproic acid (hyperammonemia)

Source: Kalish VB et al, *Am Fam Physician* 2014;90(3):150–158

3. New-onset gait disturbances could indicate Wernicke's encephalopathy, normal pressure hydrocephalus (NPH), drug toxicity, or a stroke.

Skin

1. Jaundice suggests liver disease.
2. Dry or rough skin is seen in hypothyroidism.
3. Darkened or bronzed skin could mean Addison's disease.
4. Small, reddish-purple spots beneath the skin's surface can signify a number of medical problems, including life-threatening infections.
5. Keep an eye out for drug patches. Some, like fentanyl or scopolamine (anticholinergic), can contribute to AMS (Smith and Han, 2019).

Differential diagnosis

Delirium in an older adult is often due to a combination of factors. It's helpful to tailor your workup by thinking systematically through medical and psychiatric contributors. Assess for medication and substance use by reviewing medication lists (including over-the-counter products), consulting data from prescription drug monitoring programs, checking drug levels, and obtaining alcohol/urine toxicology screens. Other diagnoses to consider include infections, metabolic/electrolyte abnormalities, nutritional deficiencies, non-convulsive status epilepticus, or structural causes.

Several psychiatric disorders can also cause AMS. See "Differential Diagnosis for Confusion" table for three of the most common psychiatric disorders to cause AMS. In addition to these, consider depression, apathy, and catatonia.

Labs and imaging

While it may be tempting to "throw the kitchen sink" at the patient, it's often better to order a standard workup and add studies as needed. Customary labs include:

1. Complete blood count. Look for anemia and thrombocytopenia. Elevated white blood cells (WBC) could indicate an infection, though keep in mind that older adults don't always have a WBC response when sick.
2. Basic metabolic panel (BMP). Pay attention to sodium levels and ionized calcium. Kidney dysfunction can arise from dehydration.
3. Fingerstick glucose. While glucose is part of the BMP, the results won't be available right away. A fingerstick will help you immediately check for hypoglycemia, which if present can be quickly reversed with orange juice or crackers.
4. Liver function tests. Consider adding an ammonia level if other signs of liver impairment are present.
5. Urinalysis and culture. UTIs are a common cause of delirium in older adults. However, this population also frequently has asymptomatic bacteria in the urine, which aren't thought to cause delirium.
6. Urine toxicology and alcohol levels. Toxicology tests, though, are prone to both false negatives and false positives.
7. Vitamin B_{12}, folate, and vitamin D levels.
8. Thyroid-stimulating hormone. Both hyper- and hypothyroidism can cause AMS in older adults (Smith and Han, 2019).

In select cases, I might also consider:

- Syphilis and HIV
- EKG, cardiac enzymes
- Chest x-ray
- Antinuclear antibody test
- Lumbar puncture
- Electroencephalogram (EEG)
- Head CT/brain MRI

Differential Diagnosis for Confusion			
	Delirium	**Dementia**	**Psychosis**
Core Feature	Inattention	Memory loss	Break with reality
Onset	Acute	Insidious	Variable
Course	Fluctuating	Chronic, progressive decline	Chronic, with exacerbations
Duration	Hours to months	Months to years	Months to years
Consciousness	Altered	Normal	Normal
Attention	Impaired	Normal in early stages	Normal
Orientation	Fluctuating	Impaired	Normal
Hallucinations	Visual	Variable	Auditory
Medical Conditions or Drug Toxicity	Present	Usually absent	Usually absent

CARLAT VERDICT

Delirium is not uncommon in older adults and may be due to multiple causes. A systematic approach allows for prompt identification and treatment.

Q&A With the Expert

Structural Brain Changes: How Imaging Affects Management of Late-Life Psychiatric Conditions

Olusola Alade Ajilore, MD, PhD

Associate professor, Department of Psychiatry, University of Illinois College of Medicine, Chicago, IL.

Dr. Ajilore, expert for this educational activity, is an employee of KeyWise AI and an advisor for Embodied Labs, Blueprint, and Sage Therapeutics. All of the relevant financial relationships listed for this individual have been mitigated.

CGPR: When do you decide to order imaging for your older adult patients?

Dr. Ajilore: I order imaging when I think there is a nonpsychiatric cause for the patient's symptoms. This could be normal pressure hydrocephalus, vascular disease including lacunar infarcts or stroke, trauma, or (in rare cases) a brain tumor. In patients with dementia, one imaging study (preferably magnetic resonance imaging [MRI]) is warranted to rule out any other cause of cognitive decline. Although imaging can help clarify the diagnosis, it may not affect management. In some ways we can get more information from extensive neuropsychological testing, which probes cognitive abilities, memory, attention, executive function, etc.

CGPR: What is the advantage to imaging? Does it change outcomes?

Dr. Ajilore: I think it informs prognosis. For example, if imaging shows plaques consistent with multiple sclerosis, or a tumor, that would inform treatment and its associated outcomes.

CGPR: In patients with dementia, what should we be looking for on imaging?

Dr. Ajilore: We are looking for patterns of brain atrophy. If the atrophy is predominantly in the prefrontal cortex, this would be more characteristic of frontotemporal dementia (FTD). If it's later on in a disease, like advanced Alzheimer's disease (AD) or the more recently recognized limbic-predominant age-related TDP-43 encephalopathy (LATE), imaging can capture atrophy in parts of the brain like the medial temporal lobe. *(Editor's note: LATE is a recently defined novel dementia characterized by hyperphosphorylated TDP-43. It damages many of the areas also affected by AD, resulting in similar symptoms. LATE is estimated to cause 15%–20% of all dementias.)*

CGPR: How do you decide when to order computed tomography (CT) versus MRI?

Dr. Ajilore: CT is useful when you want information quickly. Often you see CT used in emergency room settings right after somebody comes in with a traumatic brain injury (TBI). You want to get a CT scan to see if there's a bleed or something acute. If you want more spatial resolution and detail, an MRI is always preferred.

CGPR: Radiologists often comment on white matter hyperintensities (WMH). What exactly are these?

Dr. Ajilore: These are bright spots that show up on T2-weighted MRI images of the brain, where water appears bright. They are often in various parts of the white matter; they can appear around the ventricles (periventricular WMH) or deeper in the white matter closer to subcortical regions. You can think of white matter as representing the highways connecting different brain regions. WMH is a marker of impairment in the integrity of the white matter. It can be the result of hypertension, smoking—basically all kinds of cerebrovascular risk factors. Getting older is also associated with having more WMH. There's a strong association between having WMH and the development of some late-life conditions, such as major depression and vascular dementia.

CGPR: If you see WMH on imaging, how does this information help? Would you say a patient with WMH is at higher risk for depression? Of course, you're going to control vascular risk factors regardless.

Dr. Ajilore: I think it's something that you want to monitor. In a large European study that imaged older folks and then followed them for a couple of years, those with higher levels of WMH were more likely to develop depression (Teodorczuk A et al, *Br J Psychiatry* 2007;191:212–217). If I had a patient with no psychiatric symptoms but a high level of WMH, I would be careful about monitoring for symptoms—not just for depression, but also for cognitive symptoms.

CGPR: Are there cases in which you don't recommend imaging because it might harm the patient more than it would help?

Dr. Ajilore: Imaging is probably pretty harmless; in fact, sometimes you might incidentally discover findings that allow you to intervene early. Whenever I order a test, I take the time to discuss the results and all of the implications to minimize the patient's anxiety. Harms can occur when patients obtain imaging without proper clinical context. Without a clinician to interpret radiological findings, it is easier to make false assumptions about anomalies on imaging. However, I would say the biggest barrier to routine imaging is the cost.

CGPR: We discussed indications for structural imaging. When do you order functional MRI (fMRI)?

Dr. Ajilore: Although fMRI is widely used in psychiatric research, we don't have enough valid and reliable tools for functional neuroimaging for psychiatric conditions. We use fMRIs for neuro-navigation to find the optimal site of stimulation for repetitive transcranial magnetic stimulation (rTMS).

CGPR: What are your thoughts about using positron emission tomography (PET) scans and dopamine transporter (DaT) scans to differentiate among dementias?

Dr. Ajilore: A DaT scan visualizes striatal dopamine transporters and can be very useful in patients who have concerns about Parkinsonian symptoms. PET scans have ligands for amyloid and tau that are very useful in determining whether a patient is at increased risk for converting from mild cognitive impairment to AD. PET imaging with C-Pittsburgh

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Compound B was found to predict the conversion with 93.5% pooled sensitivity and 56.2% specificity (Zhang S et al, *Int J Clin Pract* 2012;66(2):185–198). In recent years we've seen the development of plasma markers for amyloid and tau. I think these might be more widely used because they only require a blood draw.

CGPR: Can you walk us through a case where you would order a functional study to help with the diagnosis?

Dr. Ajilore: I had a patient with Parkinsonian symptoms. She didn't quite meet criteria for Parkinson's disease, but she had Parkinsonism, and so she got a DaT scan to rule out frank Parkinson's. Her imaging showed that she didn't have the reduction in dopamine that we'd expect to see in Parkinson's disease, which helped to rule out the diagnosis.

CGPR: Have you ordered a fluorodeoxyglucose PET (FDG-PET) scan to differentiate between AD and FTD?

Dr. Ajilore: When I was at UCLA, we regularly ordered PET scans for patients in our geriatric evaluation clinic for that purpose. You see a distinct pattern of activity and hypometabolism for FTD versus AD (Foster NL et al, *Brain* 2007;130(Pt 10):2616–2635). We did use it there, although FTD can be diagnosed clinically as well. *(Editor's note: Medicare covers FDG-PET scans for the differential diagnosis of patients who meet diagnostic criteria for both FTD and AD.)*

CGPR: In a complicated case with diagnostic uncertainty, do you recommend ordering neuroimaging, or do you prefer watchful waiting to monitor for the progression of symptoms?

Dr. Ajilore: At UCLA, we used neuroimaging early in the evaluation process for our older patients with severe cognitive or behavioral disturbances. We would order imaging if there was diagnostic uncertainty that imaging might help resolve. However, many times imaging may not help you resolve this uncertainty.

CGPR: Can you give an example of how imaging affected management of one of your patients?

Dr. Ajilore: I recently treated a patient in his mid-50s who had severe impulsivity and aggression that would appear randomly, seemingly unprovoked. We learned from his history that he was, unfortunately, a victim of TBI. Imaging showed that he had a lesion in his ventrolateral prefrontal cortex—the area which governs judgment, response inhibition, and impulsivity. By revealing the location of the lesion, imaging helped us understand that the lesion could lead to his psychiatric presentation. We also realized that there's a limit to what we could do medication-wise and tempered our expectations in terms of prognosis. Recognizing that he had an injury that would make him prone to behavioral problems helped us also consider behavioral interventions and contextual changes to reduce his aggressive and impulsive behavior.

"If I'm considering vascular dementia or Alzheimer's disease (AD), I would not order imaging—this may only be sorted out through pathology. But I may order imaging if I'm uncertain whether a patient has frontotemporal dementia or AD, as there are distinct patterns I could see."

Olusola Alade Ajilore, MD, PhD

CGPR: Would you order imaging to distinguish between types of dementia?

Dr. Ajilore: If I'm considering vascular dementia or AD, I would not order imaging—this may only be sorted out through pathology. Often you see mixed pictures in the imaging that won't help you distinguish one versus the other. You can have a patient with AD that has evidence of cerebrovascular disease that's more consistent with vascular dementia, or you can have a patient that has a lot of cerebrovascular disease, but only on autopsy will you be able to note a significant amyloid and tau burden consistent with AD. But I may order imaging if I'm uncertain whether a patient has FTD or AD, as there are distinct patterns I could see on imaging.

CGPR: What results would necessitate repeat imaging?

Dr. Ajilore: If you find a lesion or condition where there might be expected change, like a tumor, you want to follow longitudinally and repeat imaging. You might even monitor WMH to see if they're increasing dramatically over time. If there is a drastic change in a patient's condition, repeat imaging may be warranted, as a significant change in the degree of atrophy or new lesions may provide a reason for the clinical change. However, tracking atrophy over time doesn't necessarily change management.

CGPR: What do you do when family members request repeat imaging when you know it won't change management? I'm thinking specifically about monitoring atrophy.

Dr. Ajilore: I would try to provide context because atrophy isn't the whole picture. Imaging provides context for what we might be seeing clinically. In fact, sometimes patients and families feel a sense of relief if we can identify a reason why they're experiencing memory loss, depression, or some other cognitive or affective symptom. Rather than making people feel anxious, imaging may provide relief and explanation. I would explain what we found on imaging within that context. If there are no unexpected changes in the patient's condition, and the degree of cognitive decline is customary for their neurocognitive disorder, I tell family members that there's nothing to be gained from another neuroimaging scan.

CGPR: The US has very high healthcare expenditures. We are very quick to order laboratory studies and imaging. How do you feel we're doing in terms of making better choices based on imaging?

Dr. Ajilore: I have only practiced in academic medical centers, and we've always been as evidence-based as possible when making our clinical decisions. As I work in a public state-funded institution, we have to be judicious about how we use our limited resources. I see commercial settings where people can pay out of pocket for tests that may not have any clinical utility. Clinics issue unsubstantiated claims and make a lot of money doing imaging procedures that have high cost and little clinical utility.

CGPR: Thank you for your time, Dr. Ajilore.

Research Updates IN PSYCHIATRY

DEMENTIA

Annual Flu Vaccines and Dementia Risk

Thomas Jordan, MD. Dr. Jordan, author of this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

REVIEW OF: Wiemken TL et al, *Vaccine* 2021;39(39):5524–5531

STUDY TYPE: Retrospective cohort study

A growing body of literature links various vaccinations (eg, diphtheria, tetanus, polio, and influenza) to a lower risk of dementia through unclear mechanisms—one theory is that vaccines activate microglia, which clear amyloid-beta. However, many of these studies are small or geographically limited.

In this study, researchers analyzed Veterans Health Administration (VHA) records of 123,747 veterans age 65 years and older without dementia from 2011 to 2019 (covering seven influenza seasons) to examine the association between influenza vaccination and incident dementia. Records of Medicare claims and Part D pharmacy claims were also included to catch any diagnoses of dementia that might have occurred outside VHA care. This sample was overwhelmingly White (91%) and male (96%).

The number of annual influenza vaccinations received was compared to incidence of dementia over the study period. 54% of the study sample received at least one influenza vaccination; the study did not differentiate between standard and high-dose vaccinations. The researchers controlled for confounding factors including physical and psychiatric comorbidities, as well as the use of medications associated with cognitive function. The overall incidence of any type of dementia was 13% over the eight-year study period.

The study found that patients who received six or more influenza vaccinations had a 12% lower risk of developing dementia compared to those who did not receive any influenza vaccinations. The mechanism behind this association is speculated to involve the vaccines training the immune system to generate nonspecific protection.

CARLAT TAKE

Similar to other vaccinations, there appears to be a link between influenza vaccination and a lower dementia risk. However, association is not causation, and many confounding factors exist in this type of retrospective research. For example, missing vaccinations could be a marker of early memory issues that later become full-blown dementia. In addition, people who are engaged in preventive care are more likely to take better care of their physical health, thus impacting modifiable risk factors for dementia. As annual influenza vaccinations are already highly recommended for elderly patients, we can continue to encourage our patients to get their annual flu shots.

DEPRESSION

Low Vitamin B_{12} Associated With Depression in Older Adults

Talya Shahal, MD. Dr. Shahal, author of this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

REVIEW OF: Laird E et al, *Br J Nutr* 2021;1–22

STUDY TYPE: Prospective cohort study

Deficiencies of both vitamin B_{12} and folate are highly prevalent among older adults. Depending on the study, 5%–40% of adults older than 50 years have B_{12} deficiency. Folate deficiency ranges from 1.2% among older adults in countries that mandate folate fortification (such as the US) to 31% in countries without this policy (such as the UK). Low concentrations of both B_{12} and folate have been correlated with depression in cross-sectional studies; this recent large longitudinal study adds to the evidence base.

The Irish Longitudinal Study on Aging followed 3,849 people who were all at least 50 years old. At baseline, participants underwent measurements including B_{12} and folate levels, as well as depression screenings with the Center for Epidemiological Studies Depression Scale (CES-D-8); they were reevaluated after two and four years. Participants with deficient-low B_{12} status at baseline (<185 pmol/L) were 51% more likely to develop depression over four years. There was no association between folate status and depression. These findings remained robust after controlling for physical activity, chronic disease burden, vitamin D levels, cardiovascular disease, and antidepressant use.

CARLAT TAKE

Checking a B_{12} level in older adults is reasonable, especially given the high rates of B_{12} deficiency in this population. Supplementation is a low-cost intervention that may decrease a patient's risk for depression.

Carlat Publishing News

Updates on some additional resources we're working on:

The Carlat Psychiatry Report: The August issue explores ADHD; upcoming topics include psychotherapy in psychiatric practice as well as depression.

The Carlat Hospital Psychiatry Report: The summer issue covers minimizing the use of restraints, while an upcoming issue tackles paraphilic disorders.

The Carlat Addiction Treatment Report: The July/August issue covers addiction and personality disorder; upcoming topics include both cannabis and trauma.

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1. What percentage of older adults admitted for depression experience delusions (LO #1)?
   [ ] a. 5% [ ] b. 20% [ ] c. 45% [ ] d. 60%

2. Which characteristics of borderline personality disorder were found to persist throughout the course of a 10-year study (LO #2)?
   [ ] a. Excessive gambling
   [ ] b. Impairment in social functioning
   [ ] c. Excessive drinking
   [ ] d. Deliberate self-harm

3. Which of the following is true regarding positron emission tomography (PET) scans (LO #3)?
   [ ] a. They are used in emergency room settings right after somebody comes in with a traumatic brain injury
   [ ] b. They can visualize striatal dopamine transporters and can be very useful in patients who have concerns about Parkinsonian symptoms
   [ ] c. They are used to find the optimal site of stimulation for repetitive transcranial magnetic stimulation
   [ ] d. They are very useful in determining whether a patient is at increased risk for converting from mild cognitive impairment to Alzheimer's disease

4. According to a 2021 study of dementia, the risk of developing dementia was lowered by how much in patients who received six or more influenza vaccinations compared to those who did not receive any influenza vaccinations (LO #4)?
   [ ] a. 5% [ ] b. 20% [ ] c. 12% [ ] d. 56%

5. In patients with delirium, which skin symptom is associated with hypothyroid-induced altered mental status (LO #1)?
   [ ] a. Darkened or bronzed skin
   [ ] b. Jaundice
   [ ] c. Small, reddish-purple spots
   [ ] d. Dry or rough skin

6. What is the one-year prevalence of bipolar disorder in adults 65 years and older (LO #2)?
   [ ] a. 9.0% [ ] b. 0.1% [ ] c. 5.2% [ ] d. 0.4%

7. Which of the following imaging tools was found to predict the conversion from mild cognitive impairment to Alzheimer's disease with 93.5% pooled sensitivity and 56.2% specificity (LO #3)?
   [ ] a. C-Pittsburgh Compound B-PET scan
   [ ] b. Functional magnetic resonance imaging
   [ ] c. Dopamine transporter scan
   [ ] d. Frontotemporal dementia PET scan

8. In a 2021 study of older adults with depression, what association did researchers find between vitamin B_{12} and depression (LO #4)?
   [ ] a. Participants with low vitamin B_{12} levels at baseline had a 51% increased likelihood of developing depression over four years
   [ ] b. Participants with high vitamin B_{12} levels at baseline had a 10% decreased likelihood of developing depression over four years
   [ ] c. Participants with average vitamin B_{12} levels at baseline had a 38% increased likelihood of developing depression over four years
   [ ] d. There was no association between vitamin B_{12} levels and depression

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The 3 Ds of Geriatric Psychiatry: Depression, Dementia, and Delirium

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mortality. If an antipsychotic was initiated during an episode of delirium, I try to taper or discontinue the medication once symptoms resolve.

I recommend low-dose melatonin or ramelteon for sleep. Cholinesterase inhibitors do not have a role in the prevention or treatment of delirium, although they can be continued in patients already taking them for dementia. Benzodiazepines, which are deliriogenic, are the preferred treatment for benzodiazepine or alcohol withdrawal.

Finally, I educate family members about the symptoms of delirium and explain how delirium can wax and wane for weeks to months, depending on the severity of the underlying medical condition. To manage expectations, I often mention how patients may or may not return to their cognitive baseline.

CARLAT VERDICT

Features of depression, dementia, and delirium overlap and may occur simultaneously. The time course of symptom onset may help you the most in diagnosing correctly. A thorough evaluation, history, and collateral from family can highlight which symptoms are taking center stage.

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