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Debunking Five Misconceptions in Agitation in Alzheimer's Dementia

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This medical industry feature, titled "Debunking Five Misconceptions in Agitation in Alzheimer's Dementia," is sponsored by Otsuka and Lundbeck.

Drs. Jackson and Patel are paid consultants of Otsuka Pharmaceutical Development & Commercialization, Inc and Lundbeck.

And now, here's Dr. Clay Jackson and Dr. Amita Patel.

Dr. Jackson:
Welcome to ReachMD. I'm Dr. Clay Jackson, a Clinical Assistant Professor of Family Medicine and Psychiatry at the University of Tennessee College of Medicine in Memphis. I'm joined by my colleague, Dr. Amita Patel, and today, we'll be discussing five common misconceptions about agitation in Alzheimer's dementia. I'm looking forward to our discussion today, Dr. Patel.

Dr. Patel:
Likewise, Dr. Jackson. Hi my name's Dr. Amita Patel, and I'm a Geriatric Psychiatrist in private practice as well as in long-term care and assisted living facilities in Dayton, Ohio. I see misconceptions about agitation in Alzheimer's dementia pretty often in clinical practice, so I'm glad to have this opportunity to set the record straight.

Dr. Jackson:
Thank you, Dr. Patel, and with that in mind, let's jump right in. I want to begin with the prevalence of agitation in Alzheimer's dementia, and why it's important to recognize it as more than just symptom changes.

You know, Alzheimer's dementia isn't just about memory loss—there are a variety of neuropsychiatric symptoms that can occur in the disease, and agitation is one of the most common of those neuropsychiatric symptoms, with a significant clinical impact.[1]

In fact, 76 percent of patients with Alzheimer's dementia will develop it.[2] And while agitation is a symptom, it's still a separate, treatable condition from Alzheimer's.[3,4]

But agitation may not look the same in each patient. And because it presents in different ways, it's often underdiagnosed and undertreated. Despite its high prevalence, less than five percent of patients receive formal diagnosis codes, creating a "silent epidemic" where most of the patient suffering goes unrecognized by the healthcare system.[1,5]

Dr. Patel:
That's a great place to start. A lot of people assume agitation equals aggression, but you are correct, the way agitation presents can be broader and more complex than some clinicians may realize and can manifest with both aggressive and nonaggressive symptoms.[1,6] We often think first of more obvious symptoms like hitting or physical outbursts like yelling, screaming, pushing or throwing objects, but agitation can be more subtle and may therefore not be recognized. According to the International Psychogeriatric Association, or IPA, criteria, agitation shows up in three core ways: excessive motor activity, verbal aggression, or physical aggression.[6]

Increased motor activity can look like pacing, rocking, restlessness, or repetitive behaviors, and verbal symptoms can include shouting, complaining, repetitive questioning, or using an excessively loud voice.[6]

The IPA also emphasizes that agitative symptoms represent a clear – and often dramatic – change from a patient's usual baseline and are tied to emotional distress. So if we only recognize agitation when it becomes physical, then we may miss opportunities to intervene sooner and reduce the distress both for the patient and the caregiver. And while the symptoms may not seem severe at first – but over time, they become exhausting and disruptive to daily life.[6]

The Cohen-Mansfield Agitation Inventory, or the CMAI, is a clinically validated scale that evaluates the frequency of 29 different agitated behaviors and allows for the assessment of each symptom individually.[7] One study that used the CMAI to measure the frequency and disruptiveness of agitative symptoms in nursing home residents with dementia found that the more frequently a symptom occurs, the more disruptive it tends to be. While the physically aggressive symptoms were the most disruptive overall, even verbally nonaggressive symptoms—like repetitive questioning or complaints— can have a significant impact when they happen repeatedly.[8]

So these symptoms may sound harmless, but they should not be ignored because they represent a real impact of agitation.

Dr. Jackson
That's right, and I'd just like to point out that the Cohen-Mansfield study was conducted in a nursing home setting, where continuity of observation is a strength.[8] Because agitation can be episodic and may present differently across settings, a traditional brief office visit rarely tells the whole story, and this can be a real challenge for those of us who are in primary care.[3,4]

Because of that, clinicians often depend on caregiver input to understand what's happening outside the clinic. Caregivers are often the first ones to notice subtle symptom changes. With that being said, they may not recognize the full breadth of agitation symptoms or even realize that agitation is a symptom of the disease. As you mentioned, Dr. Patel, these symptoms can take a toll on caregivers—but caregivers may not discuss them until it becomes unmanageable.[9]

This creates a gap – clinicians are relying on caregiver reporting, but caregivers may not recognize or communicate early symptoms, especially when those symptoms are non-aggressive and subtle. So what ends up happening is that both sides may miss opportunities for earlier recognition. And that's why it's *so* important for clinicians to regularly ask caregivers about specific behavior changes and patterns over time rather than relying solely on what emerges during a visit.[9]

Tools like the Agitation in Alzheimer's Screener for Caregivers, or AASC, can support this process by helping caregivers recognize agitation symptoms early and discuss observations with clinicians during visits. It's great because it's just a one page document, and there are additional resources available on the AASC website that can help support caregivers and clinicians working together to better recognize and monitor agitation in patients with Alzheimer's dementia.[9] These tools can enhance conversations and move us beyond the traditional, unassisted office visit.

Dr. Patel:
I agree, Dr. Jackson. That's an excellent point and an important reminder to listen closely to the people who see the patients every day.

Another misconception is that agitation symptoms are associated with cognitive decline or inherent aspect of Alzheimer's dementia, but that's not necessarily true.[4,10]

Cognitive decline associated with Alzheimer's dementia is characterized by memory loss, confusion, and steady progressive impairment, which is driven by amyloid and tau-related pathology.[4,10]

Agitation is thought to result from a functional imbalance between the "top-down" executive control from the prefrontal cortex, or the PFC, and the "bottom-up" emotional drive from the amygdala. This imbalance is driven by disruption in key neurotransmitter systems—specifically the norepinephrine, serotonin, and dopamine—which are also impacted by pathological accumulation of beta amyloid plaques and tau proteins associated with Alzheimer's. These neurotransmitters may therefore represent a key targets for the potential improvement of agitation symptoms in Alzheimer's dementia.[3,10]

In addition, while cognitive decline in Alzheimer's dementia is progressive and continuous, agitation is episodic and fluctuating, and can be triggered or worsened by modifiable external triggers such as environment or stress.[3,4]

So distinguishing cognitive decline and agitation as separate conditions rather than an inevitable part of Alzheimer's dementia is really important, because the treatment approaches are different. Alzheimer's therapies slow or treat cognitive decline, while managing agitation involves both identifying external triggers and addressing the neurotransmitter imbalances.[3,4]

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Today, Dr. Clay Jackson and Dr. Amita Patel are discussing five common misconceptions about agitation in Alzheimer's dementia.

Dr. Jackson:
Now that we have discussed agitation in Alzheimer's dementia, let's talk about management. As you were saying, Dr. Patel, because cognitive decline and agitation are different facets of Alzheimer's dementia, they can't be treated as one entity.[3,10]

Alzheimer's dementia involves cognitive, neuropsychiatric, and functional components that *don't* stem from the same biology. That's why they can't be managed in the same way.[10-13]

For example, some traditional Alzheimer's disease drugs target cholinergic and glutaminergic pathways to help cognitive function.[10,11] Agitation, however, is more closely linked to monoaminergic dysfunction, including norepinephrine, serotonin, and dopamine.[10,11] This helps explain why medications developed to delay cognitive decline may not address agitation—and in some cases, may even worsen neuropsychiatric symptoms including agitation.[14-16] As for newer anti-amyloid therapies, their effects on neuropsychiatric symptoms are less well-studied.[17,18]

So all of this tells us that it's not a one-size-fits all treatment approach—we need something more targeted for each pathophysiological mechanism. There is FDA-approved treatment for agitation in Alzheimer's dementia, including one drug classified as an atypical antipsychotic. However, clinicians may prescribe other unapproved medications.[10,19]

Taken together, this reinforces an important point: agitation is not an extension of cognitive decline—it has a distinct mechanism and requires its own treatment strategy.[3,10,11,13]

Historically, management of agitation often involved the off-label use of certain psychotropic medications like antipsychotics, benzodiazepines, or anxiolytics. Unfortunately, these medications can carry a significant risk profile, including—but not limited to—sedation.[20]

And that brings us to our final misconception. From a clinical standpoint, Dr. Patel, why is sedation an inappropriate therapeutic goal?

Dr. Patel:
Well, quieter doesn't equal better. Achieving sedation is not the same as treating agitation.[20-23]

Patients may appear calmer or quieter, but that's often a side effect of psychotropic medications—not an improvement in agitation and actually represents an adverse effect rather than a therapeutic outcome.[20-23] And that distinction matters, because sedation can come with real downsides—less engagement in activity, more withdrawal, higher risk of falls and fractures, cognitive decline and lower quality of life.[20,21,24,25]

Current CMS guidelines for long-term care are very clear that psychotropic medications should only be used when clinically indicated, properly documented, and after nonpharmacological approaches have been tried and have failed to gain adequate control of agitation.[26]

More broadly though, this isn't unique to CMS. Across guidelines, the general recommendation is to start with nonpharmacologic strategies and only consider medication if those measures are ineffective or symptoms are severe, dangerous, and or significantly distressing.[9,26]

For example, in my experience in other settings—like assisted living—we may take a more proactive approach to managing agitation. So, I think the underlying principle of CMS guidelines remain relevant across all care settings, because the use of medication primarily for sedation may be considered a form of chemical restraint.[26]

The primary treatment goal should be reducing agitation symptoms while preserving engagement, alertness, functioning, and quality of life.[20,21,27]

Dr. Jackson:
I agree. With any disease, our goal should be to address the underlying pathology when possible—in this case, the neurotransmitter imbalance—not to simply mask the symptoms.

And with those final thoughts in mind, I'd like to thank Dr. Amita Patel for sharing her insights in recognizing and managing agitation in Alzheimer's dementia. Dr. Patel, I really enjoyed our conversation today.

Dr. Patel:
I couldn't agree more. A big thanks as well to Dr. Clay Jackson for sharing his perspective on this important topic.

Announcer:
This medical industry feature was sponsored by Otsuka and Lundbeck. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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May 2026 US.CORP.X.26.00020