

New research focuses on treating non-cognitive symptoms of people with dementia

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Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

New research presented at the Alzheimer's Association International Conference (AAIC) 2018 in Chicago focuses on the recent successes and ongoing challenges of drug and non-drug treatments for the non-cognitive symptoms experienced by people living with Alzheimer's dementia.

While the memory and thinking symptoms associated with the disease are the most well known, it is the behavioral and psychological symptoms of [dementia](#) (BPSD)—agitation, anxiety, apathy, depression, wandering, hallucinations, insomnia, incontinence, disinhibition—that

often cause the greatest caregiving challenges and are the leading causes for placement in assisted living or nursing homes. Left untreated, these symptoms can accelerate decline and reduce quality of life.

At this time, the U.S. Food and Drug Administration (FDA) has not approved any drug treatments for these symptoms in people with Alzheimer's dementia. All drug treatments currently used are approved for other indications and prescribed for people with Alzheimer's "off-label."

"These underrecognized and undertreated symptoms in people with Alzheimer's and other dementias are often very difficult to live with and challenging to treat," said Maria Carrillo, Ph.D., Alzheimer's Association Chief Science Officer. "One of the 'untold stories' of Alzheimer's is the regular occurrence and overwhelming impact of these symptoms on the lives of people with Alzheimer's, their family members and caregivers."

"It is very important that as we continue to make advances in treating and preventing the memory and thinking symptoms of Alzheimer's and other dementias, we also focus on therapeutic strategies for the behavioral and other non-cognitive symptoms," Carrillo added.

The Alzheimer's Association recommends non-pharmacologic approaches such as psycho-social interventions as first-line alternatives to pharmacologic therapy for the treatment of dementia-related behaviors. These therapies include validation therapy, reminiscence and other personalized psychosocial interventions.

For example:

- Validate that the person seems to be upset over something.
- Separate the person from what seems to be upsetting.
- Engage in regular physical activity to potentially reduce

irritability and aggressive behavior.

- Assess for the presence of pain, constipation or another physical problem.

Psychotropic medications (antipsychotics, antidepressants, anticonvulsants and others) may need to be considered when the dementia-related behavior has not responded to non-pharmacologic approaches, especially if it is causing physical or emotional harm to the person with dementia or caregiver(s), however they must be used with extreme care, and must be regularly evaluated to determine the appropriate time of cessation. The FDA found that using antipsychotics to treat dementia-related behaviors in elderly persons with dementia was associated with increased mortality.

Synthetic Cannabinoid Treatment Shows Improvement in Agitation in People with Alzheimer's

Results of a randomized, double-blind clinical trial suggest that nabilone—a synthetic cannabinoid—may be effective in treating agitation in people with Alzheimer's disease. "Agitation, including verbal or physical outbursts, general emotional distress, restlessness, pacing, is one of the most common behavioral changes associated with Alzheimer's as it progresses, and can be a significant cause of caregiver stress," said Krista L. Lanctôt, Ph.D., Senior Scientist at Sunnybrook Health Sciences Centre and Professor of Psychiatry and Pharmacology/Toxicology at the University of Toronto.

Lanctôt and colleagues investigated the potential benefits of nabilone for adults with moderate to severe Alzheimer's dementia with clinically significant agitation. Over the 14-week trial duration, 39 participants (77 percent male, average age 87) received nabilone in capsule form (mean therapeutic dose=1.6 +/- .5 mg) for six weeks, followed by six weeks of

placebo, with one week between each treatment period. In addition to measuring agitation, the researchers assessed overall behavioral symptoms, memory, physical changes and safety. They found that:

- Agitation improved significantly in those taking nabilone, compared to placebo, as measured by the Cohen-Mansfield Agitation Inventory ($p=0.003$).
- Nabilone also significantly improved overall behavioral symptoms, compared to placebo, as measured by the Neuropsychiatric Inventory ($p=0.004$).

The researchers also observed small benefits in cognition and nutrition during the study. More people in the study experienced sedation on nabilone (45 percent) compared to placebo (16 percent).

"Currently prescribed treatments for agitation in Alzheimer's do not work in everybody, and when they do work the effect is small and they increase risk of harmful side effects, including increased risk of death. As a result, there is an urgent need for safer medication options," said Lanctôt. "These findings suggest that nabilone may be an effective treatment for agitation; however, the risk of sedation must be carefully monitored. A larger clinical trial would allow us to confirm our findings regarding how effective and safe nabilone is in the treatment of agitation for Alzheimer's."

Note: Marijuana is not approved by the FDA for the treatment or management of Alzheimer's disease or other dementias. As medical marijuana use becomes more common, it is important to point out that much about its use in people with Alzheimer's or other dementias is unknown.

Marijuana is, essentially, an untested drug in Alzheimer's. There is currently no robust, consistent clinical trial data supporting the use of

marijuana for treatment of Alzheimer's disease dementia—nor for related issues. The Alzheimer's Association believes that more research in this area is needed.

Lighting May Improve Sleep, Mood and Behavior in People with Alzheimer's

Many people living with Alzheimer's disease and other dementias experience changes in their sleep patterns, insomnia, and daytime sleepiness. Mariana G. Figueiro, Ph.D., Director of the Lighting Research Center at Rensselaer Polytechnic Institute in Troy, NY, and colleagues tested whether a tailored lighting system could help to improve sleep, mood and behavior in people with Alzheimer's disease in nursing homes.

"Given that light/dark patterns are a person's primary cues to the current time, the constant dim light typically experienced by people living in residential care facilities may be an underlying cause of the sleep pattern disturbances so commonly found in this population," said Figueiro.

To test this hypothesis, over a four-week period, lighting interventions were placed in areas where nursing home residents spent the majority of their waking hours and were left on from wake-up time until 6 p.m. Forty-three (43) residents (31 female, 12 male) participated in the short-term study, and 37 residents (25 female, 12 male) have completed the long-term study so far, all recruited from 10 [nursing homes](#) in the New York Capital District, Bennington, VT, and South Bend, IN.

Study participants experienced alternating periods of lighting that provided either high- or low-circadian stimulus for four weeks (short-term study) and six months (long-term study, successive four-week periods spaced by a four-week washout). The circadian stimulus (CS)

metric, developed by the Lighting Research Center, characterizes a light source's effectiveness for stimulating the circadian system as measured by its capacity for acutely suppressing the body's production of the hormone melatonin (a well-established marker of the circadian system) after a one-hour exposure.

Both arms of the study used either a custom-designed LED light table or individual room lighting to deliver the intervention, depending on where the participants spent the majority of their time. Personal light meters were used to measure the light exposures received at the participants' eyes. Sleep disturbance, mood and agitation were also assessed using standardized questionnaires.

With the lighting intervention, researchers found that study participants who experienced the high-circadian stimulus showed significant decrease in sleep disturbance, depression and agitation. Positive effects observed in the short-term study continued to improve over the long-term study.

Beyond Anti-Psychotics: Exploring Efficacy and Harms of Z-Drugs for Sleep Disturbance

Many people with dementia have problems sleeping. This affects their quality of life and that of the people who care for them. Non-benzodiazepine hypnotic "Z-drugs," such as zolpidem, zopiclone and zaleplon, are often prescribed to help treat insomnia in older adults, but it is thought that they may cause problems such as falls, fractures, and increase confusion. People living with dementia are especially vulnerable and it is not clear whether Z-drugs are particularly harmful for them.

Chris Fox, MD, Professor of Psychiatry at Norwich Medical School University of East Anglia in Norwich, U.K., and colleagues analyzed

existing data from the UK Clinical Practice Research Datalink, and from three clinical studies of people with dementia. They compared data for up to two years for 2,952 people with dementia who were newly prescribed Z-drugs with data for 1,651 who were not, in order to evaluate the benefits and harms of these medicines.

They found that the use of Z-drugs is associated with a 40 percent increased risk of any type of fracture, with risk increasing for those on higher doses. Z-drug use was also associated with a greater risk specifically of hip fracture. The study did not identify a higher risk of other effects, such as falls, infections or stroke.

"Fractures in people with dementia can have a devastating impact, including loss of mobility, increased dependency and worsening dementia," said Fox. "We desperately need better alternatives to the drugs currently being prescribed for sleep problems and other non-cognitive symptoms of dementia. Wherever possible, suitable non-pharmacological alternatives should be considered, and where Z-drugs are prescribed, patients should receive care that reduces or prevents the occurrence of falls."

Provided by Alzheimer's Association

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