

Long-term caffeine worsens anxiety symptoms and fear of the new associated with Alzheimer's disease

3 April 2018

A study coordinated by the Institute of Neuroscience of the Universitat Autònoma de Barcelona (Inc-UAB) and in collaboration with the Karolinska Institutet (KI) in Sweden provides evidence that a long-term consumption of caffeine has negative effects for Alzheimer's disease, worsening the neuropsychiatric symptoms appearing in the majority of those affected by the disorder. The research was recently published in *Frontiers in Pharmacology*.

Memory problems are the hallmark of Alzheimer's [disease](#). However, this dementia is also characterised by [neuropsychiatric symptoms](#), which may be observed in the earliest stages of the disorder. Known as behavioural and psychological symptoms of dementia (BPSD), the symptoms include anxiety, apathy, depression, hallucinations, paranoia and sundowning. They are considered the strongest source of distress for patients and caregivers.

Coffee or caffeine has recently been suggested as a strategy to prevent dementia, both in patients with Alzheimer's disease and in normal ageing processes, due to its action in blocking molecules – adenosine receptors – which may cause dysfunctions and diseases in old age. However, there is some evidence that once the cognitive but also the NPS symptoms are developed, caffeine may exert opposite effects.

To address these issues, the study was conducted with normal ageing mice and familial Alzheimer's models. "The mice develop Alzheimer's disease similarly to human patients with an early-onset form of the disease. They not only exhibit the typical cognitive problems but also a number of BPSD-like symptoms, so it is a valuable model to address whether the benefits of caffeine will be able to compensate its putative [negative effects](#),"

says Raquel Baeta-Corral, first author of the research.

"We had previously demonstrated the importance of the adenosine A1 receptor as the cause of some of caffeine's adverse effects. Now, we have simulated a long oral treatment with a very low dose of caffeine (0.3 mg/mL) equivalent to three cups for a human coffee-drinker to answer a question relevant for patients with Alzheimer's, but also for the ageing population in general, and that in humans would take years to be solved since we should wait until the patients were aged," says Dr. Björn Johansson, researcher and physician at the Karolinska University Hospital. The research was conducted from the onset of the disease to more advanced stages. Healthy, age-matched mice provided control data.

The results indicate that caffeine alters the behaviour of healthy mice and worsens the neuropsychiatric symptoms of mice with Alzheimer's disease. The researchers discovered significant effects in the majority of variables studies, especially in relation to neophobia, a fear of everything new, anxiety-related behaviours, and emotional and cognitive flexibility.

In [mice](#) with Alzheimer's disease, the increase in neophobia and anxiety-related behaviours exacerbates their BPSD-like profile. Learning and memory, strongly influenced by anxiety, got little benefit from caffeine.

"Our observations of adverse caffeine effects in an Alzheimer's disease model together with previous clinical observations suggest that an exacerbation of BPSD-like symptoms may partly interfere with the beneficial cognitive effects of [caffeine](#). These results are relevant when coffee-derived new potential treatments for dementia are to be devised

and tested," says lead researcher Dr. Lydia Giménez-Llort of the INC-UAB Department of Psychiatry and Legal Medicine.

More information: Raquel Baeta-Corral et al. Long-term Treatment with Low-Dose Caffeine Worsens BPSD-Like Profile in 3xTg-AD Mice Model of Alzheimer's Disease and Affects Mice with Normal Aging, *Frontiers in Pharmacology* (2018).
[DOI: 10.3389/fphar.2018.00079](https://doi.org/10.3389/fphar.2018.00079)

Provided by Autonomous University of Barcelona
APA citation: Long-term caffeine worsens anxiety symptoms and fear of the new associated with Alzheimer's disease (2018, April 3) retrieved 21 May 2019 from
<https://medicalxpress.com/news/2018-04-long-term-caffeine-worsens-anxiety-symptoms.html>

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