

D-galactose affects aging male and female brains differently

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A study coordinated by the UAB and in collaboration with the ULL reveals the biological relevance of sex in the alteration of behaviour and the neuro-immuno-endocrine system, caused by accelerated aging with a chronic treatment of D-galactose, a sugar found abundantly in milk and in some fruits and vegetables. The research was recently published in the *Journal of Gerontology: Biological Sciences and Medical Sciences*.

For almost two decades, chronic treatments with D-galactose have been used as a tool to create animal models of accelerated aging. Their neurotoxicity is due to abnormal ROS accumulation, molecules proper of oxidative stress and AGEs, proteins or lipids which become glycated as a result of exposure to sugars, both related to the acceleration of multisystem functional decline occurring during aging. These D-galactose-induced biological products are also involved in the development or deterioration of many degenerative diseases such as diabetes, arteriosclerosis, kidney diseases, infections and Alzheimer's disease.

"The difficulty in research with accelerated aging models using D-galactose lies in the fact that its neurotoxicity effects at the biochemical level do not always translate into pathological symptoms at the behavioural level. In the study, we found convincing evidence of some of them, and observed important differences between the males and females," says Dr. Lydia Giménez-Llort, lead researcher of the project.

Through a complete and multifunctional behavioural analysis, the

researchers examined the chronic effects of low (50 mg/kg) and high (100 mg/kg) doses of D-galactose in male and female mice aged six months—the equivalent of 40 human years. Based on the results of 12 tests, they assessed the sensory, motor, emotional and cognitive fields, and also explored the effects on the neuro-immuno-endocrine system, decisive in pinpointing the vital capacity or [biological age](#) of individuals.

The results point to the existence of different sensitivity thresholds depending on the sex of the animal with regards to their functional capacity to meet the performance level required for certain tasks: D-galactose had pro-aging effects at the sensory and motor levels and on the immuno-endocrine system in males, while it altered motor performance and some learning processes as well as their spatial memory in females.

"The most surprising results are found in the low doses of D-galactose, which seem to trigger positive effects in males, such as improved learning and memory, while in females, the expected dose-response ratio continues, with deteriorated motor and spatial learning, although there are improvements in some aspects such as memory. These results point to the complexity of the effects at functional level, and therefore all of these observations open the door to new lines of research which can clarify all these underlying neuronal mechanisms and help to understand the vulnerability and differential protection observed," explains Dr. Rafael Castro, ULL researcher and co-author of the study.

"In the past few years, what is known as gender-specific medicine advises the need and importance to research sex and gender-specific aspects, as well as the age factor, and creating more personalised medicines. Our study demonstrates this need and reinforces the idea that the male and female genders must be considered two exceptional natural scenarios in which to study the biological, psychological, social and environmental roles, their functional interactions and their impact on the

intercommunication of homeostatic networks, which guarantee a balance in health and are affected by diseases throughout their life cycle," Dr. Giménez-Llort says.

The research also contributes to gaining more in-depth knowledge in the study of biological and environmental determinants, as well as lifestyles and habits at specific moments such as in mid-life, in which the aging process gains speed and gradually reduces the organism's functional capacities, which begin to see a limitation in their biological antioxidant capacity to counteract imbalances caused by age.

More information: Raquel Baeta-Corral et al, Sexual Dimorphism in the Behavioral Responses and the Immunoendocrine Status in D-Galactose Induced Aging, *The Journals of Gerontology: Series A* (2018). [DOI: 10.1093/gerona/gly031](https://doi.org/10.1093/gerona/gly031)

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