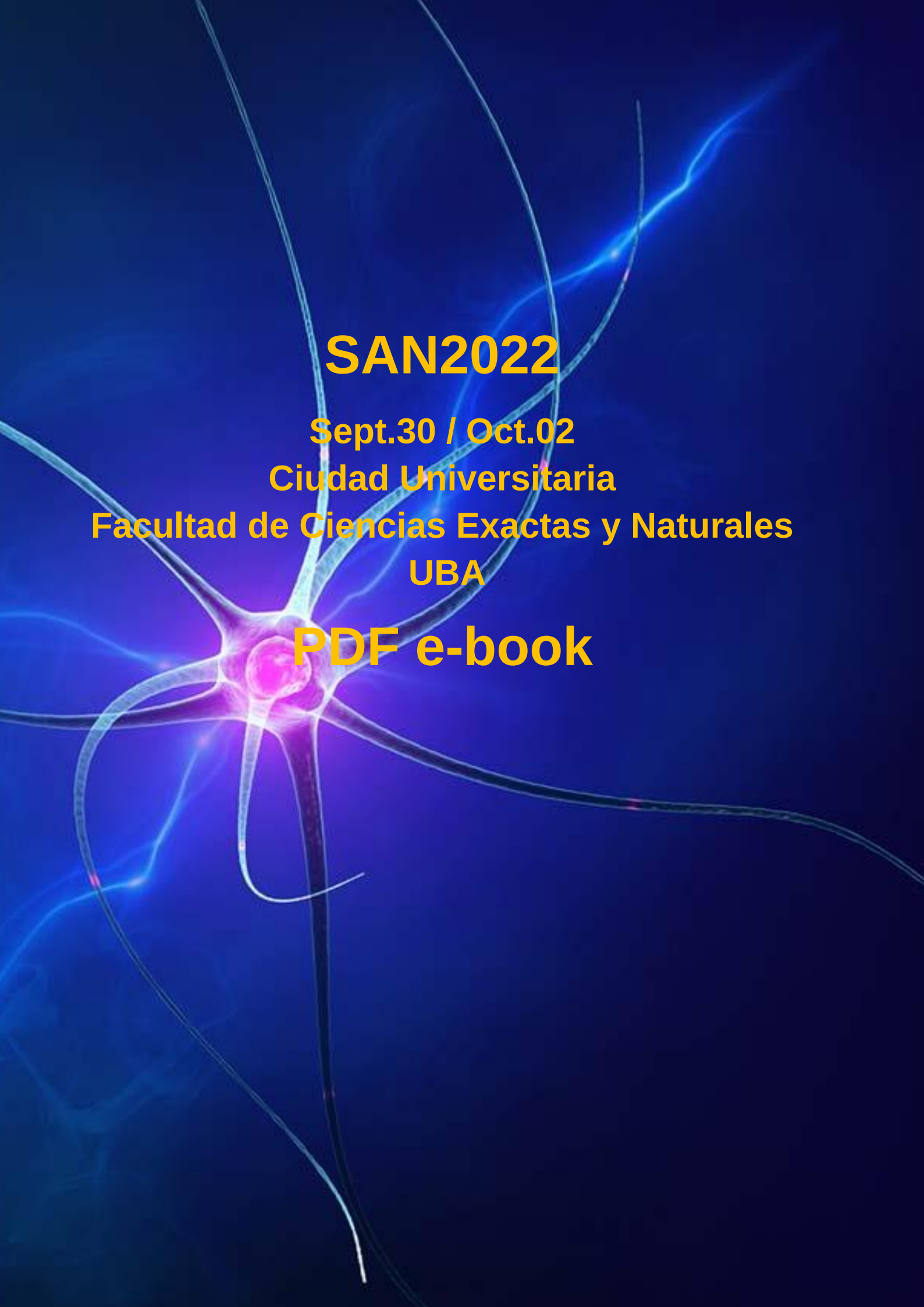

SAN2022

Sept.30 / Oct.02

Ciudad Universitaria

Facultad de Ciencias Exactas y Naturales

UBA

PDF e-book

157 | Ferroptosis in midbrain triggers motor impairment associated with lipid dyshomeostasis

Disorders of the Nervous System

Author: Melisa Conde | email: mconde@inibibb-conicet.gob.ar

Melisa Conde [2°*], Athina Maniscalchi [1°*], Oriana Benzi Juncos [2°], Eugenia Fermento [2°], Alejandro Curino [2°], María Marta Fachinetti [2°], Melania Funk [2°], Natalia Alza [3°], Gabriela Salvador [2°]

1° Instituto de Investigaciones Bioquímicas de Bahía Blanca, Universidad Nacional del Sur (UNS), Consejo Nacional de Investigaciones Científicas y Técnicas.
2° Instituto de Investigaciones Bioquímicas de Bahía Blanca, Universidad Nacional del Sur (UNS), Consejo Nacional de Investigaciones Científicas y Técnicas, Departamento de Biología, Bioquímica y Farmacia, UNS.
3° Instituto de Investigaciones Bioquímicas de Bahía Blanca, Universidad Nacional del Sur (UNS), Consejo Nacional de Investigaciones Científicas y Técnicas, Departamento de Química, UNS

Ferroptosis is a form of cell death driven by iron-dependent phospholipid peroxidation by means of antioxidant defense failure related with glutathione depletion. It has major implications in many neurodegenerative diseases. Previously, our laboratory demonstrated that iron overload triggers neurodegeneration and exacerbated lipolysis in whole brain. The goal of this work was to characterize the effect of ferroptosis as a consequence of iron overload in mice midbrain. C57BL/6 mice were intraperitoneally injected with iron saccharate (200 or 333 mg/kg weight) to generate an iron overload model. We found that iron was accumulated in midbrain of treated mice through Perls' staining. This was correlated with higher levels of oxidative stress markers, lipid peroxidation and glutathione depletion, with no changes in caspase activity. Remarkably, tyrosine hydroxylase loss and increased gliosis were detected in midbrain slices of iron-treated animals. Lipid metabolism alterations were also investigated. While fatty acid levels were diminished, cholesterol content was increased by iron overload. Iron-treated animals displayed reduced falling latency and total distance travelled in the rotarod and open field tests, respectively. Our findings indicate that our model represent a scenario of ferroptosis in midbrain with cholesterol accumulation that affects motor skills.

*Equal contribution