

Accelerated Accumulation Of Neuronal DNA Damage In An Obese Rat Model: Implications For Brain Aging And Reduced Lifespan

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Take-home Message:

Obesity may make the young brain biologically older by accelerating neuronal DNA damage.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Obesity is increasingly linked with accelerated brain ageing and higher vulnerability to neurodegenerative disease. Beyond amyloid and tau pathology, obesity-associated metabolic stress may promote genomic instability in neurons. DNA damage in cognition-related brain regions may therefore represent an early molecular signal of obesity-driven brain ageing. Aim: To determine whether obesity accelerates neuronal DNA damage in the neocortex and hippocampus of WNIN/Ob obese rats, and whether this damage resembles age-related genomic deterioration.	WNIN/Ob obese rats were compared with age-matched WNIN lean littermates and normal WNIN controls. Animals were studied at 3 months and 15 months of age. DNA strand breaks were assessed in the neocortex and hippocampus using comet assay under alkaline and neutral conditions to measure single-strand and double-strand DNA damage.	Young WNIN/Ob obese rats showed markedly increased neuronal DNA damage in both the neocortex and hippocampus. The damage pattern in young obese rats was comparable to that seen in aged normal WNIN rats. In contrast, young lean littermates and normal controls showed lower and comparable levels of DNA damage. Keywords: Obesity; neuronal DNA damage; brain ageing; hippocampus; neocortex; genomic instability; Alzheimer’s disease; WNIN/Ob rat.	Obesity was associated with premature neuronal DNA damage in brain regions essential for cognition and memory. These findings suggest that obesity may accelerate molecular features of brain ageing and contribute to reduced lifespan and increased neurodegenerative vulnerability. The WNIN/Ob rat may serve as a useful model for studying obesity-linked brain ageing and Alzheimer’s disease risk.	Sinha et al., 2014, <i>Neuroscience</i> Ghosh et al., 2019, <i>IJMR</i> Potukuchi et al., 2018, <i>Nutri Neuroscience</i> Welch & Tsai, 2022, <i>EMBO Reports</i> Azam et al., 2021, <i>Frontiers in CDB</i> Collins, 2004, <i>Molecular Biotechnology</i> Olive & Banáth, 2006, <i>Nature Protocols</i> Flores-Cordero et al., 2022, <i>IJMS</i> CONTACT  Dr. Jitendra Kumar Sinha, Symbiosis International (Deemed University), Pune, Maharastra, India ALZHEIMER'S ASSOCIATION 