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ROTENONE-INDUCED OXIDATIVE STRESS TRIGGERS PEROXISOMAL ALTERATIONS IN BV-2 MICROGLIAL CELLS

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Peroxisomes are small, single-membrane organelles, essential for cellular homeostasis. Originating via fission or de novo from the endoplasmic reticulum, they possess specialized enzymatic machinery for several metabolic pathways. In cooperation with mitochondria, peroxisomes regulate lipid metabolism and redox balance. Within the central nervous system, they support neuroglial functions and modulate immune pathways linked to neurodegeneration.

This study investigates how oxidative stress induced by the pesticide rotenone (Rot), a mitochondrial toxin, impacts the peroxisomal compartment in BV2 microglial cells, aiming to elucidate peroxisomes contribution within a Parkinsonian-like neuroinflammatory context.

Rot treatment triggered a pro-inflammatory microglial phenotype, characterized by morphological changes, cytoskeletal disruption and oxidative damage to biomolecules. Notably, Rot induced a robust peroxisomal response, characterized by marked organelle proliferation, enlargement, and redistribution towards the perinuclear region. Consistent with such adaptive strategy, Rot exposure activated antioxidant defences and coordinated a metabolic shift towards enhanced lipid catabolism. The depletion of lipid droplets supports an increased reliance on peroxisome-dependent fatty acid processing as a critical survival mechanism under conditions of redox imbalance.

Overall, these findings underscore the remarkable plasticity of the peroxisomal compartment, demonstrating their capacity to cope with mitochondrial damage through morpho-functional remodelling. Peroxisomes engage an active, yet insufficient, adaptive response to fully restore homeostasis under sustained Rot-induced stress. These observations suggest that targeting peroxisomal pathways could serve as a potential strategy to mitigate the energetic dysmetabolism and neuroinflammatory processes associated with Parkinson's Disease.

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