The cause of dopaminergic cell death in Parkinson’s Disease (PD) is unknown, but recent research demonstrates oxidative stress, inflammation, and the endogenous neurotoxin, 3,4-dihydroxyphenylacetaldehyde (DOPAL), are factors in PD pathogenesis. DOPAL is generated from dopamine (DA) by monoamine oxidase and oxidized to DOPAC, the acid metabolite, by aldehyde dehydrogenase. DOPAL is highly toxic to dopaminergic cells and must be rapidly metabolized to avoid toxicity. Interaction of DOPAL with non-neuronal cells (e.g., microglia), including metabolism, activation, and toxicity is unknown. Activated microglia, found in PD-affected areas of the brain, can damage dopaminergic cells through phagocytosis, ROS and proinflammatory cytokine production/release. The ability of DA and metabolites to activate BV-2 microglia was shown in this work by TNF-α release. Metabolism and toxicity of DOPAL were determined for BV-2 cells, and it was found microglia metabolize DA to DOPAC via DOPAL. A known product of lipid peroxidation, malondialdehyde, inhibited DOPAL catabolism, as did pre-activation of the cells. Aggregation of the PD-relevant protein, α-synuclein, by physiologically relevant levels of DOPAL was also demonstrated in this work. DOPAL-mediated microglial activation as shown in this study represents a viable mechanism for inflammation and dopaminergic cell death seen in PD patients.