The dopamine metabolite aminochrome inhibits mitochondrial complex i and modifies the expression of iron transporters DMT1 and FPN1

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Hallmarks of idiopathic and some forms of familial Parkinson's disease are mitochondrial dysfunction, iron accumulation and oxidative stress in dopaminergic neurons of the substantia nigra. There seems to be a causal link between these three conditions, since mitochondrial dysfunction can give rise to increased electron leak and reactive oxygen species production. In turn, recent evidence indicates that diminished activity of mitochondrial complex I results in decreased Fe-S cluster synthesis and anomalous activation of Iron Regulatory Protein 1. Thus, mitochondrial dysfunction could be a founding event in the process that leads to neuronal death. Here, we present evidence showing that at low micromolar concentrations, the dopamine metabolite aminochrome inhibits complex I and ATP production in SH-SY5Y neuroblastoma cells differentiated into a dopaminergic phenotype. This effect is apparently direct, since it is replicated in isolated mitochondria. Additionally, overnight treatment wit