

DNA damage precedes cell death in rotenone rat model of Parkinson's disease

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Introduction

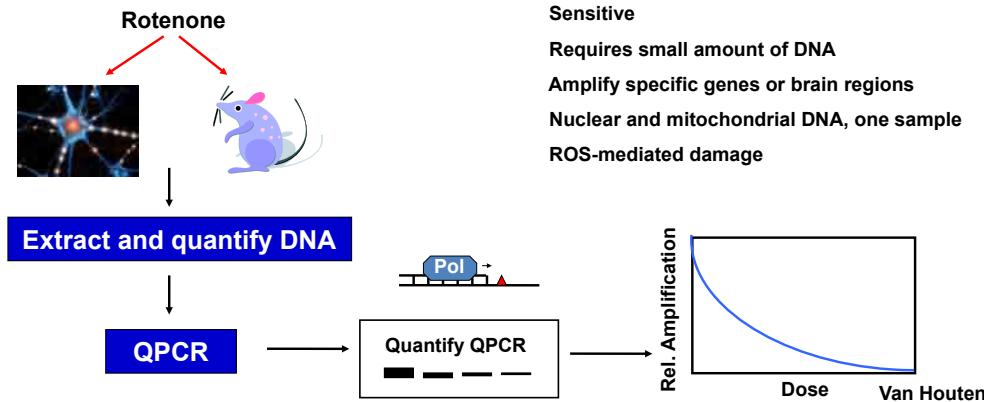
Parkinson's disease (PD) is a progressive neurodegenerative disorder that is characterized in part by loss of neurons of the substantia nigra. The initial trigger(s) for neuronal cell death in PD remains elusive. Mitochondrial function is impaired in PD and is associated with oxidative stress, which may damage macromolecules. Previous reports have suggested increased DNA damage and mitochondrial mutations in the substantia nigra of PD patients; however it is unclear when DNA damage occurs during the neurodegenerative process.

Hypothesis

We hypothesize that DNA damage is an early event in dopaminergic cell loss in the substantia nigra.

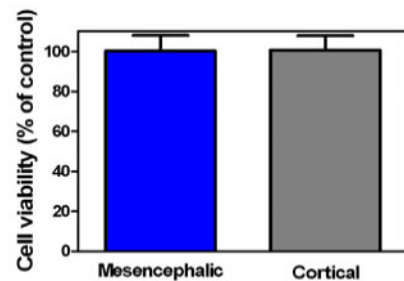
Methods

Quantitative PCR assay

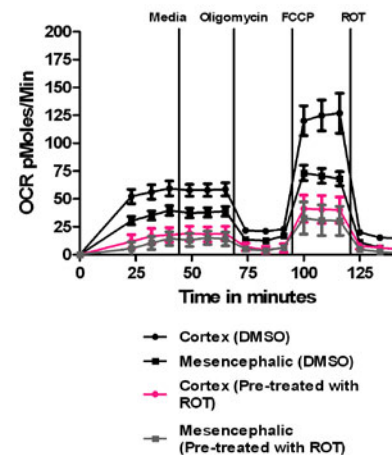


Results

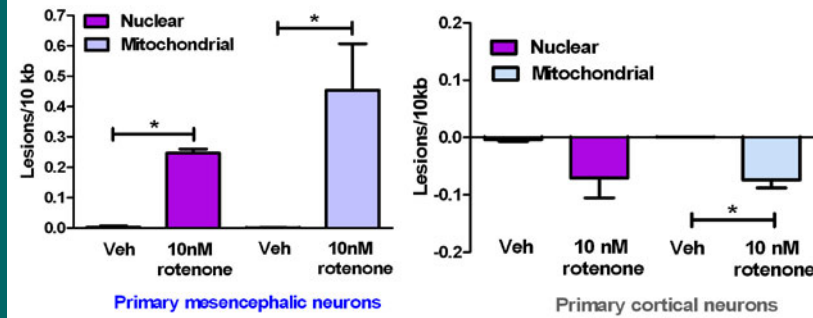
1. Primary neuronal cultures treated with 10nM for 24h is sublethal.



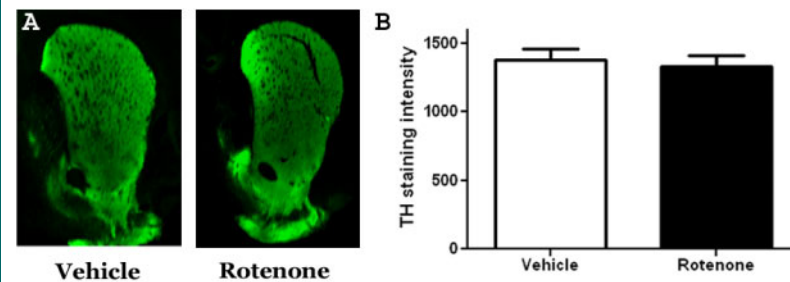
Rotenone inhibits mitochondrial respiratory function equally in primary mesencephalic and cortical neurons.



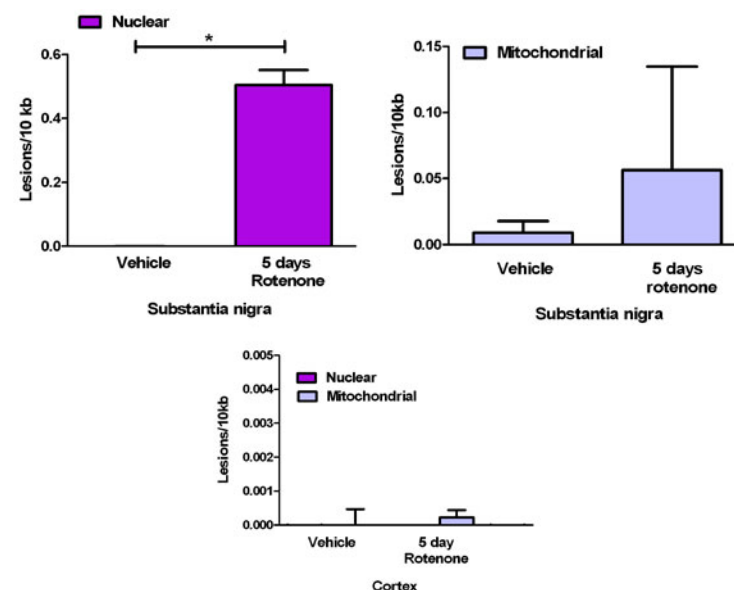
2. Sublethal rotenone treatment selectively induces nuclear and mitochondrial DNA damage in mesencephalic neurons.



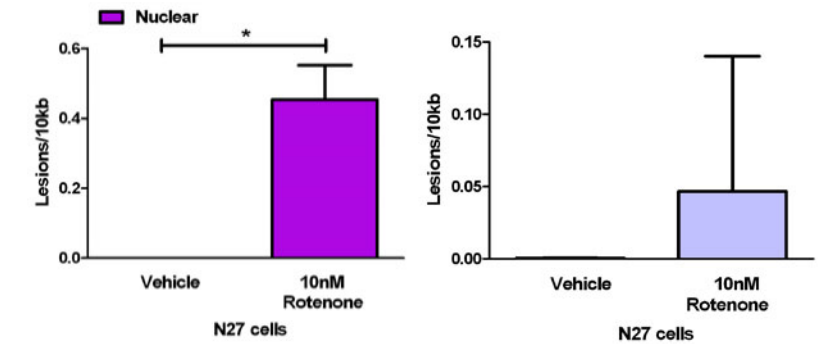
3. We chose a dose (3mg/kg/day) and time (5 days) where there is no striatal TH lesion *in vivo*.



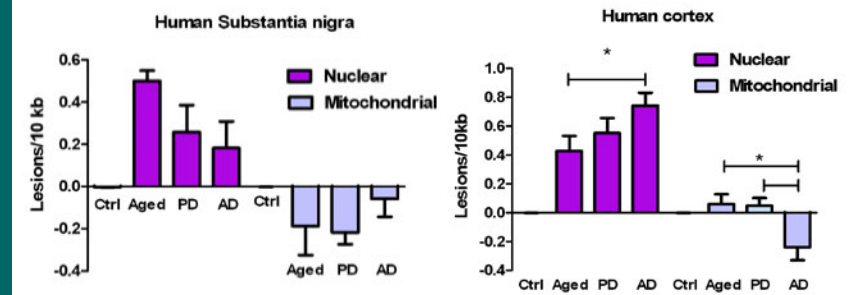
4. Rotenone-induced selective nuclear and mitochondrial DNA damage in substantia nigra *in vivo*.



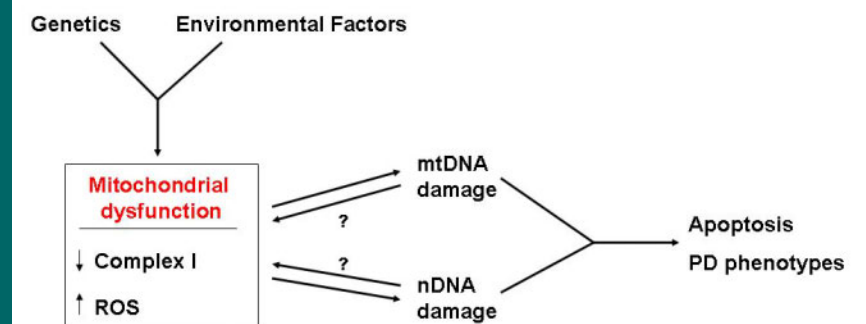
5. DNA damage in the dopaminergic N27 cell line is similar to observed DNA damage in substantia nigra *in vivo*.



6. DNA damage in human PD and AD substantia nigra and cortex brain tissue.



Summary



Acknowledgements

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