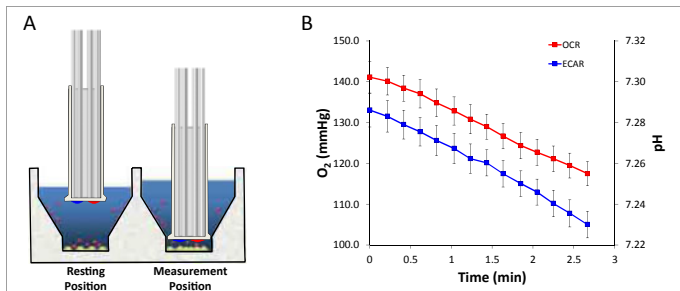
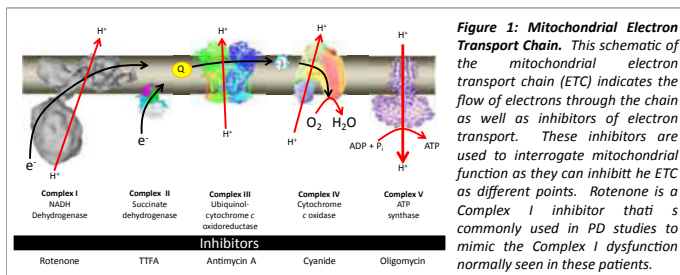
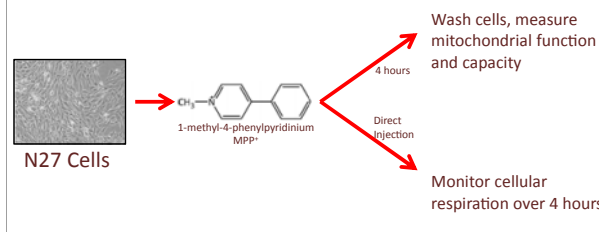


Introduction

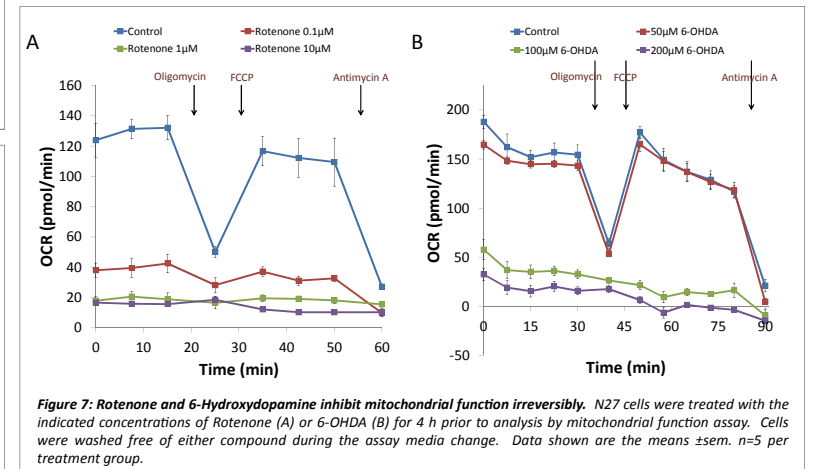
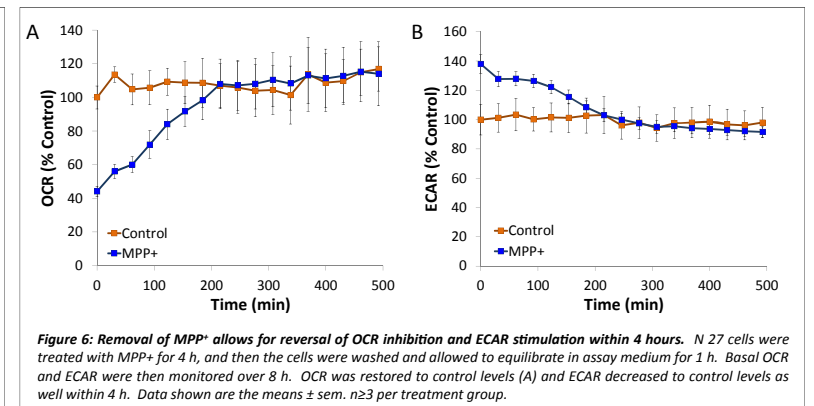
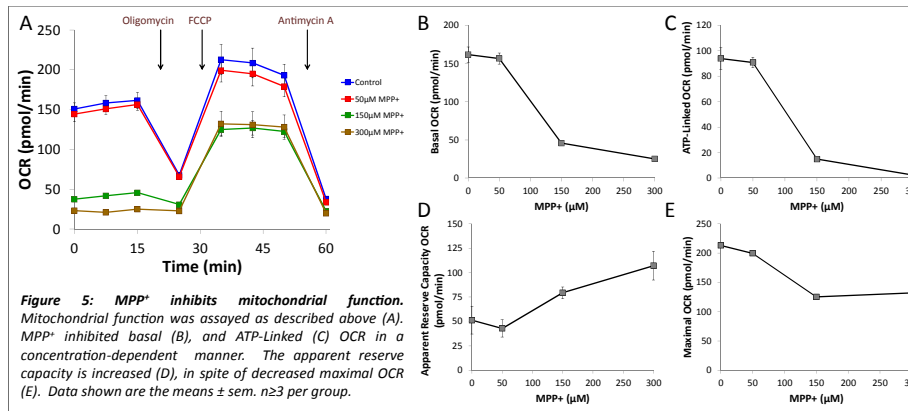
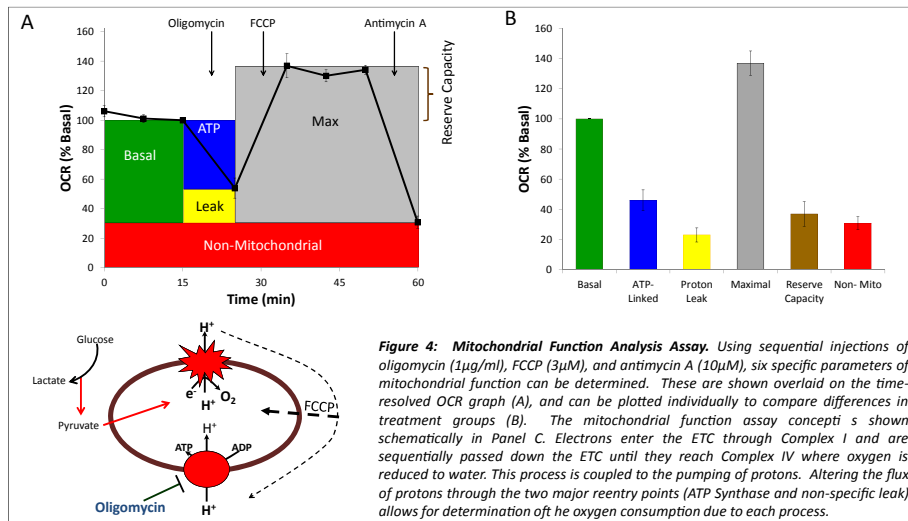
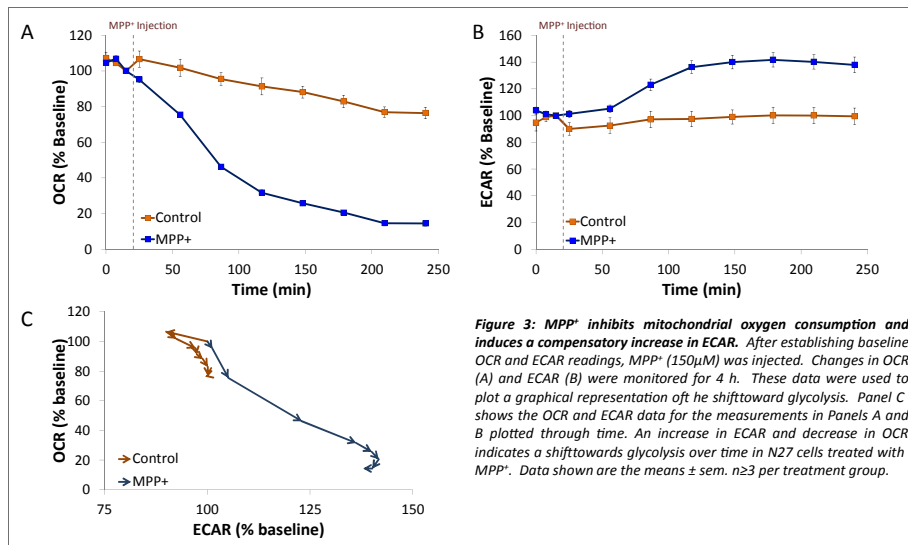
- Mitochondrial dysfunction is clearly recognized as a hallmark of neuronal failure in Parkinson's disease. Inhibition of mitochondrial Complex I is thought to be the main contributor to this dysfunction.
- 1-methyl-4-phenylpyridinium (MPP⁺), the ultimate toxic metabolite of the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), has been used in cultured cells to inhibit Complex I and induce cell death, but its effects on cellular energy utilization are not well-defined.
- We hypothesized that sublethal MPP⁺ treatment would lead to a decrease in the bioenergetic function of immortalized rat mesencephalic N27 cells prior to cell death.
- In this study, cellular bioenergetic function was quantified using a Seahorse Bioscience XF24 Extracellular Flux Analyzer. A modified protocol for monitoring mitochondrial function was used.¹ Cellular glycolytic function was also assessed.

Methods

Experimental Design



Results



Conclusions

- Treatment with 300 μ M MPP⁺ decreased the basal OCR to 21.0 \pm 3.1 pmol/min from 102.4 \pm 2.4 pmol/min.
- Non-mitochondrial oxygen consumption following MPP⁺ treatment was not significantly different, indicating that the cells were not subject to an acute oxidative stress.
- In response to the inhibition of mitochondrial respiration, we also found that the Extracellular Acidification Rate, used as a marker of glycolysis, increased in concert with OCR inhibition.
- Together these data indicate that MPP⁺ dramatically shifts bioenergetic function away from the mitochondria and towards glycolysis in N27 cells.

References

- Dranka BP, Hill BG, Darley-Usmar VM. Mitochondrial reserve capacity in endothelial cells: the impact of nitric oxide and reactive oxygen species. Free Radic Biol Med. 2010 Apr 1; 48(7):905-14.

This work is supported by NIH grant NS039958 and the Harry R. & Angeline E. Quadracci Chair Endowment (both to B.K.)