

# 1,3-Dinitrobenzene Inhibits Mitochondrial Complex II in Rat and Mouse Brainstem and Cortical Astrocytes

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## Abstract

1,3-Dinitrobenzene (DNB) produces edematous, glio-vascular lesions that are initially confined to brainstem nuclei with high energy requirements in rats and mice. Perturbation of energy producing processes in the cell is known to induce formation of the mitochondrial permeability transition pore (mtPTP) complex. Selective vulnerability of brainstem astrocytes to DNB is mediated by a 10-fold lower threshold for opening of the cyclosporin A-inhibitable mitochondrial permeability transition (MPT) pore than their cortical counterparts. Other nitrocompounds, such as 3-nitropropionic acid, selectively interfere with regional energy metabolism, including mitochondrial succinate dehydrogenase activity. However, the link between DNB-induced onset of the MPT and disruption of energy producing processes in the astrocyte remains unclear. The effects of DNB on succinate dehydrogenase activity were evaluated in cultured neonatal rat and mouse brainstem and cortical astrocytes. Both histochemical and spectrophotometric assays confirmed significant temporal inhibition of SDH activity in brainstem and cortical astrocytes 0.5, 2 and 5 h following exposure to 100  $\mu$ M DNB *in vitro*. Although DNB-induced inhibition of SDH was significantly decreased by CsA pretreatment in brainstem astrocytes after 0.5 and 2 h and with a second pore inhibitor, bongkreikic acid (BKA) after 5 h, both inhibitors failed to reduce inhibition of SDH activity in cortical astrocytes. These data suggest that DNB-induced inhibition of SDH may be independent of differential regional activation of the mtPTP complex in astrocytes and that an unidentified cyclosporin A-inhibitable factor mediates DNB-induced loss of SDH function.

**Keywords:** Mitochondrial complex II; Succinate dehydrogenase; Astrocytes; Dinitrobenzene