

Effects of guanethidine on electron transport and proton movements in rat heart, brain and liver mitochondria

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Guanethidine at 5-25 mM concentrations was found to induce up to 79% inhibition of ADP-stimulated (state III) oxygen consumption in isolated rat heart, brain or liver mitochondria, when the added substrate was glutamate or succinate, but the inhibition was considerably lower (24% or less) when respiration was supported by ascorbate plus tetramethylphenylenediamine (TMPD). Comparable results were seen regarding ADP-stimulated proton uptake, where even greater inhibition (up to 94% with glutamate or succinate, but not ascorbate plus TMPD) was found. Similar but somewhat less marked effects were also seen in resting (state IV) respiration and on the acceptor control ratio (state III/state IV respiration). 2,4-Dinitrophenol was unable to relieve guanethidine-induced inhibition of electron transport. These results indicate that guanethidine inhibits primarily mitochondrial electron transport itself, and that the site where such inhibition is more marked is located in the span between ubiqui