Scientific Paper:

Circulation 107, 2146-2152, 2003

Differences in the Biogenergetic Response of the Isolated Perfused Rat Heart to Selective ß$_1$- and ß$_2$-Adrenergic Receptor Stimulation

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Abstract:

Background—In the heart, striking functional differences exist after stimulation of the ß$_1$- and ß$_2$-adrenergic receptor (AR) subtypes. These may be linked to differences in metabolic response during ß$_1$- and ß$_2$-AR stimulation.
Methods and Results—The relation between work and metabolism was examined during selective ß$_1$- and ß$_2$-AR stimulation (ß$_1$ and ß$_2$ groups, respectively) in the isolated perfused rat heart. Measurements were made of rate-pressure product (RPP = LV developed pressure x heart rate), phosphorus-containing metabolites, and pH by ^{31}P nuclear magnetic resonance spectroscopy and of O_2 consumption by fiber-optic oximetry. Experiments were performed under high constant flow (HCF) and under flow-limiting conditions (constant pressure, CP). Despite substantially greater RPP increases relative to baseline during ß$_1$-AR (HCF, 475%; CP, 150%) than ß$_2$-AR (HCF, 90%; CP, 72%) stimulation, the relative decrease in the intracellular energy charge relative to baseline was similar for the ß$_1$ (HCF, 49%; CP, 64%) and ß$_2$ (HCF, 59%; CP, 55%) groups. For each group, an increase in oxygen consumption (MVo_2) occurred commensurate with workload during HCF (ß$_1$, 141%; ß$_2$, 30%). During CP, however, the MVo_2 increase was similar (ß$_1$, 39%; ß$_2$, 34%), despite the large RPP difference between the groups. During both protocols, there was greater acidosis during ß$_1$-AR than during ß$_2$-AR stimulation. Thus, at a given workload, intracellular energy charge decreased, and MVo_2 (CP) increased to a greater extent during ß$_2$ than ß$_1$-AR stimulation.
Conclusions—The bioenergetic differences are consistent with access to an additional substrate pool during ß$_1$-AR stimulation. This may occur via increased glycogenolysis during ß$_1$-AR stimulation, facilitating increased energy production by oxidative phosphorylation, and under flow-limiting conditions, anaerobic glycolysis.

Key-words: Receptors, adrenergic, beta, metabolism, oxygen, imaging