Differences in the Biogeneretic Response of the Isolated Perfused Rat Heart to Selective β₁- and β₂-Adrenergic Receptor Stimulation

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Abstract:

Background—In the heart, striking functional differences exist after stimulation of the β₁ and β₂ adrenergic receptor (AR) subtypes. These may be linked to differences in metabolic response during β₁ and β₂ AR stimulation.

Methods and Results—The relation between work and metabolism was examined during selective β₁ and β₂ AR stimulation (β₁ and β₂ 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 ³¹P nuclear magnetic resonance spectroscopy and of O₂ 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 β₁-AR (HCF, 475%; CP, 150%) than β₂-AR (HCF, 90%; CP, 72%) stimulation, the relative decrease in the intracellular energy charge relative to baseline was similar for the β₁ (HCF, 49%; CP, 64%) and β₂ (HCF, 59%; CP, 55%) groups. For each group, an increase in oxygen consumption (MVo₂) occurred commensurate with workload during HCF (β₁, 141%; β₂, 30%). During CP, however, the MVo₂ increase was similar (β₁, 39%; β₂, 34%), despite the large RPP difference between the groups. During both protocols, there was greater acidosis during β₁-AR than during β₂-AR stimulation. Thus, at a given workload, intracellular energy charge decreased, and MVo₂ (CP) increased to a greater extent during β₂ than β₁-AR stimulation.

Conclusions—The bioenergetic differences are consistent with access to an additional substrate pool during β₁-AR stimulation. This may occur via increased glycogenolysis during β₁ AR stimulation, facilitating increased energy production by oxidative phosphorylation, and under flow-limiting conditions, anaerobic glycolysis.

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