

An isolated guinea-pig working heart: preliminary studies with histamine and noradrenaline

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In 1965, Morgan, Neely, Wood, Liebecq, Liebermeister and Park, introduced an isolated, stable working heart from rats. This preparation has been used more extensively for biochemical and physiological studies (e.g. Neely, Liebermeister, Battersby & Morgan, 1967; Penpargkul & Scheuer, 1970) than for pharmacological studies.

The working heart preparation, unlike those based on the Langendorff preparation, performs external work. It also affords the measurement of aortic flow, left ventricular pressure and cardiac work in addition to sinus rate, force of contraction and coronary flow, thus allowing better characterization of changes in cardiac function. This preparation, unlike the heart-lung preparation, is completely isolated.

We have chosen to establish an isolated working guinea-pig heart as this species responds readily to cardioactive drugs such as histamine (Bartlet, 1963) and ouabain (Spilker, 1973).

Duncan Hartley guinea-pigs, of either sex, 450-600 g were killed 20 min after heparin (2000 u i.p.) and the heart excised. The aorta was cannulated and the heart perfused retrogradely for 2 min with Krebs Henseleit bicarbonate buffer equilibrated with 95% O₂/5% CO₂ at 37.5°C. During this time the left atrium was cannulated. When working, the heart was perfused via the left atrium at a pressure of 10 cm H₂O and aortic flow was pumped against a pressure head of 70 cm H₂O. Drugs were injected into the left atrial cannula, just before the heart, at a constant volume of 0.5 ml over 5 seconds.

The parameters measured were sinus rate (S.R.), left ventricular pressure (L.V.P.), and its first derivative dp/dt, aortic flow (A.F.), coronary flow (C.F.), cardiac output (C.O.) and pressure work (P.W.). Where appropriate, measurements are expressed per gram dry weight of heart.

Preparations were left to stabilize for about 25 min and used for a further 45 minutes.

After stabilization, the values for parameters were: P.W. 0.326 ± 0.013 kg-m min⁻¹ g⁻¹, L.V.P. max. 85.7 ± 1.5 mmHg, dp/dt max. 1572 ± 94 mmHg/s, S.R. 211.3 ± 4.1 beats/min, A.F. 313.0 ± 10.5 ml min⁻¹ g⁻¹, C.F. 65.9 ± 2.7 ml min⁻¹ g⁻¹ and C.O. 371.7 ± 11.8 ml min⁻¹ g⁻¹ ($n=9-16$).

Histamine injections between 1×10^{-9} mol and 3.5×10^{-8} mol produced dose-related increases in P.W., A.F. and C.O. and between 1×10^{-9} mol and 1×10^{-7} mol produced dose related increases in L.V.P. max. dp/dt max. and S.R. Effects on C.F. were small and variable. At histamine 3.5×10^{-8} mol the increases were: P.W. $54.7 \pm 4.1\%$, C.O. $23.3 \pm 7.2\%$, S.R. 37.2 ± 3.4 beats/min, L.V.P. max. $51.7 \pm 13.4\%$, dp/dt max. $127 \pm 22.2\%$, C.F. $11.0 \pm 11.1\%$ and A.F. $24.5 \pm 6.9\%$ ($n=3$).

Noradrenaline injections between 1×10^{-10} mol and 1×10^{-8} mol produced dose related increases in all measured parameters. At 1×10^{-8} mol the increases were: P.W. $46.7 \pm 7.5\%$, C.O. $29.9 \pm 7.4\%$, S.R. 67.3 ± 9.7 beats/min, L.V.P. max. $28.0 \pm 2.7\%$, dp/dt max. $138.6 \pm 21.0\%$, C.F. $29.0 \pm 2.7\%$ and A.F. $30.8 \pm 8.9\%$ ($n=3$).

These preliminary results indicate that the isolated working heart responds readily to cardiac stimulants and that this preparation is suitable for study of the effects of drugs on cardiac function.

References

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