Hepatic fructose metabolism studied by \(^{31}\)P nuclear magnetic resonance in the anaesthetized rat

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We have previously shown (Iles et al., 1980) that the metabolism of fructose may be followed in isolated rat livers by using \(^{31}\)P n.m.r. spectroscopy. The introduction of the surface-coil technique (Ackerman et al., 1980) makes it possible to study metabolism in the anaesthetized animal.

A fed male Wistar rat was anaesthetized by intraperitoneal sodium pentobarbital, catheterized in the right jugular vein and secured vertically within a 7 cm n.m.r. probe. A flat, three-turn 10 mm-diameter radiofrequency coil was placed on the surface of the left lobe of the liver through an abdominal incision. To prevent evaporation, and to electrically insulate the coil, the liver surface was covered with thin plastic film. The probe was inserted into a wide-bore Oxford Instruments superconducting (4.3 T) magnet. Radiofrequency pulses were repeated every 300 ms and blocks of 256 scans were accumulated (in 75 s) for each spectrum.

Previous work (R. A. Iles, J. R. Griffiths, A. N. Stevens, D. G. Gadian & R. Porteous, unpublished work) has demonstrated that the spin–lattice relaxation times \((T_1)\) of most phosphate-containing liver metabolites are short compared with those in other tissues (Ackerman et al., 1980). In the present study preliminary evidence shows no saturation in the signals from ATP, ADP, P\(_i\) or sugar phosphate.

Several blocks of scans were accumulated to confirm the stability of the preparation. Fructose (750 mg/kg) was then infused over 2 min while scanning was continued. The time course of each experiment was approx. 1 h.

Fig. 1(a) shows a typical spectrum before infusion of fructose and is essentially the same as was observed in isolated perfusion experiments (R. A. Iles, J. R. Griffiths, A. N. Stevens, D. G. Gadian & R. Porteous, unpublished work). Peak A contains signals from sugar phosphates, AMP, IMP and 2,3-bisphosphoglycerate, peak B from P\(_i\) and 2,3-bisphosphoglycerate, peak C from the \(\gamma\)-phosphate moiety of ATP and the \(\beta\)-phosphate moiety of ADP, peak D from the \(\alpha\)-phosphate moieties of ATP and ADP and the two phosphate moieties of NAD, and peak E from the \(\beta\)-phosphate moiety of ATP. These signals are superimposed on a broad hump, thought to derive from phospholipids (McLaughlin et al., 1979). Fig. 1(b) shows the spectrum obtained 140 s after the beginning of fructose infusion. Peak B, due to P\(_i\), is eliminated, and peak A, reflecting sugar phosphate, particularly fructose 1-phosphate, is very much larger, reaching a maximum after 8 min. Peaks E and C, due to ATP and ADP respectively, are much smaller. Comparison of these spectra, obtained with fed rats, with results obtained from 48 h-starved rats confirms the observation by Sestoft (1974) that fructose 1-phosphate accumulation is greater in fed than in starved rats. Peak D shows a smaller decline, since it includes a signal from NAD and NADP, which is presumably unaffected by fructose infusion.

Further spectra were obtained but are not shown. When the fructose 1-phosphate peak was at its maximum, 8 min after infusion, that of ATP was at its lowest (<25% of that in the control spectrum). Both fructose 1-phosphate and ATP values partially returned to their control values. After 60 min the ATP peak was 60% of the control [perhaps because of degradation of the adenylate pool to uric acid (Määnpää et al., 1968; Van den Berghe et al., 1977)]. These changes in the concentrations of intracellular metabolites are similar to those found by previous workers (Määnpää et al., 1968; Woods et al., 1970; Sestoft, 1974; Van den Berghe et al., 1977).

The surface-coil technique has advantages over previous liver n.m.r. techniques (Salhany et al., 1979; McLaughlin et al., 1979; Iles et al., 1980) in that less signal is observed from the extracellular space and that the liver need not be removed from the animal, so avoiding dangers of ischaemia.


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