by 100 μM tolbutamide. These properties resemble those of ATP-sensitive K-channels in other cells. A lower estimate of 104 channels per HIT-T15 cell is obtained from the single channel and whole cell conductances, which would be increased if the lower conductance in 5 mmol/l K_o were allowed for, suggesting that this cell-line may be a promising source of material for channel purification.

258. Muscle lipoprotein lipase activity is decreased by glucose and insulin

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The effect of a physiological increase in plasma insulin concentration on muscle lipoprotein lipase activity (LPLA), on leg exchange of glucose and on serum lipoproteins was investigated in healthy young overnight-fasted men. During euglycaemic hyperinsulinaemia (n = 7) at 40 mU/l, m-LPLA decreased from 30 mU/g w.w. to 19 ($p < 0.05$). The decrease correlated closely (r = 0.97) with the increase in leg glucose uptake, and basal m-LPLA correlated with the increase in leg glucose uptake (r = 0.93). In the control subjects (n = 7) receiving saline in place of insulin and glucose, m-LPLA was not changed with time. Insulin decreased VLDL-triacylglycerols (TG) by 47%, LDL-cholesterol (C) by 5% and HDL_2-C by 15%. As LDL-C decreased less than total HDL-C, LDL-C/HDL-C ratio increased (8%) with insulin, whereas the control subjects remained unchanged. It is concluded that in contrast to the effect on adipose tissue, physiological concentrations of insulin decrease m-LPLA in proportion to the effect of insulin on glucose uptake. Furthermore, basal m-LPLA is an indicator of muscle insulin sensitivity.

259. Long-term registration of RR intervals during the night improves diagnosis of autonomous neuropathy

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Even if all current tests for the diagnosis of autonomous neuropathy (AN) are applied, there remains residual inaccuracy (unknown actual status and patients' compliance). In 53 Type 1 (insulin-dependent) diabetic patients RR intervals have been registered automatically for 1 min from 22.00 hours to 08.00 hours every 15 min. Both the minimum (CVmin) and the maximum CV (CVmax) have been evaluated. Additionally the coefficient of variation of the RR intervals (CV) under resting conditions (CVrest) and forced respiration (CVresp) have been determined. Significant correlations:
1) CVrest = 0.67 + 1.34/CVmin (r = 0.688, $p < 0.001$),
2) CVresp = 0.31 + 3.56/CVmin (r = 0.862, $p < 0.001$),
3) CVresp = 0.30 + 0.58/CVmax (r = 0.771, $p < 0.001$). Since the slope in (1) is higher than expected, the study indicates that the determination of heartbeat variation in routine tests is markedly biased. Eq. (2) demonstrates a high predictability of CVresp by the objective measure CVmin. Only pronounced stages of AN are diagnosed correctly by measuring CVrest and CVresp; intermediate stages are underestimated.

260. Isoproterenol modulates insulin activation of insulin receptor kinase in intact rat adipocytes

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It has been shown that B-adrenergic agonists produce insulin resistance both in vivo and in vitro. We studied whether this effect might be related to an ability of isoproterenol to alter the activation of insulin receptor kinase (IRK) by insulin. Isolated rat adipocytes were preincubated for 30 min at 37 °C wtih or without isoproterenol. For activation of IRK, insulin (0–500 ng/ml) was then added and the cells incubated for an additional 15 min. Insulin receptors were subsequently isolated and immunoprecipitated in the presence of kinase and phosphatase inhibitors. IRK activity towards histone that was then measured in an assay with 0.5 μmol/l ^{32}P-ATP reflected the activity state of the receptors while the cells were intact. Insulin incubation of the cells resulted in a 20–30-fold increase in IRK activity. Compared to control cells, in cells pretreated with isoproterenol, the insulin effect on IRK was decreased by 36.8 ± 3.3%, 37.3 ± 4.5%, 27.8 ± 8.4%, and 9.6 ± 8.3% at 1, 4, 20, and 500 ng/ml insulin, respectively. In contrast, no alteration in ^{125}I-insulin binding to cells pretreated with isoproterenol was observed (0.29 ± 0.05% and 0.28 ± 0.04% per 10^5 cells at 0.2 ng/ml, in isoproterenol-treated and control cells, respectively). Our data are consistent with the view that isoproterenol modulates the coupling of insulin binding to biological actions of insulin at or before the level of activation of IRK.

261. Streptozotocin-induced Ia expression in pancreata and kidneys of mice

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It was assayed whether the expression of class II molecules, i.e. Ia antigens, is effected by administration of the diabetogen streptozotocin (STZ). BALB/c males received intraperitoneally either a single or multiple injections of STZ. Pancreata, kidneys, salivary glands and livers were removed at various time intervals after treatment and snapfrozen. Ia antigens were detected by a peroxidase-method on cryo-cut sections using a monoclonal antibody with specificity for I-A^d. A monoclonal antibody detecting Ia^k determinants was used for control. It was found that expression of Ia antigens was increased in pancreatic, kidney and salivary gland tissues after a single injection of subdiabetogenic dosages of 10, 20, or 40 mg STZ/kg body weight or after 3 or 5 injections of 40 mg STZ/kg body weight. In contrast, in liver sections no increased Ia antigen expression was observed. Furthermore, a toxic dose of 200 mg STZ/kg body weight, inoculated once, resulted in Ia antigen expression in the islets only. Interestingly, the increased class II molecule expression was detectable already 6 h after STZ treatment. The kinetics and dose-dependency of the STZ-induced increment of Ia antigen expression will be presented, the significance related to the development of hyperglycaemia discussed.

262. Cholecystokinin-modulated phospholipid metabolism and phosphoinositide breakdown in rat pancreatic islets

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The gut hormone cholecystokinin octapeptide (CCK_8) sensitises the rat pancreatic B cell to glucose acting via specific CCK receptors. The relationship between glucose- and CCK-induced insulin release and the phospholipid metabolism, phosphatidylinositol breakdown and emergence of inositol phosphates was investigated. When islets were labelled with [^{3}H]arachidonic acid for 90 min glucose decreased the incorporation of label into phosphoinositol and phosphatidylserin (PI + PS), phosphatidylcholine (PC), phosphatidylethanolamine (PE) and diphosphatidylglycerol (DPG) in a dose-dependent manner. 10 nmol/l CCK_8 increased this glucose effect with respect to PC, PE and DPG. In myo-[^{3}H] inositol prelabelled islets glucose in a dose-dependent manner increased inositol-1,4,5-triphosphate (IP_3) without affecting inositol phosphate (IP) and inositol-1,4-bisphosphate (IP_2). 10 nmol/l CCK_8 dramatically increased IP_3 and IP_2 and marginally IP, which was most prominent during the very first 3 min. This CCK effect was most prominent at 3.0 and 8.3 mmol/l glucose, but not 16.7 mmol/l. CCK_8 concomitantly decreased the source of inositolphosphates such as phosphatidylinositol 4,5-bisphosphate and phosphatidylinositol 4-phosphate. The data indicate a lower PC, PE and DPG labelling and a higher emergence of inositol phosphates probably from poly-phosphoinositides in rat pancreatic islets induced by CCK_8; this shift may be involved in the sensitising effect of islets to glucose-mediated insulin release by CCK_8.

263. In vitro non-activated mononuclear blood cells produce factor(s) which increase unstimulated insulin release

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Glucose-stimulated insulin secretion from pancreatic islets is reduced by crude cell-free supernatants of in vitro-activated (lectins, antigens) peripheral blood mononuclear cells (MNC) from healthy donors. In this study, the effect of non-activated MNC on insulin release was compared with that of their cell-free culture supernatants. Insulin release from non-glucose stimulated islets was increased by the non-activated MNC from control subjects (2.1 ± 1.4 vs 11.3 ± 7.2 ng/20 h per islet, n = 18, means ± SD) and from diabetic patients (2.2 ± 1.4 vs 11.3 ± 6.3 ng/20 h per islet, n = 24). Insulin release was also increased in a dose- and time-dependent manner by supernatants of these MNC. Maximum insulin release from 20 h incubated islets was already caused by cell-free supernatants obtained after a preincubation of 1–2 h. The effects could partially be blocked by epinephrine (3 μmol/l) and propranolol (6 μmol/l) but not by heat inactivation of the culture supernatants. Thus, the observed effect is apparently not due to an action of interleukin 1. The study supports the role of soluble factor(s) released by MNC independent of antigens mediating anti-islet immune responses in interaction with insulin secretion.