by 100 μM tolbutamide. These properties resemble those of ATP-sensitive K-channels in other cells. A lower estimate of 194 channels per HIT-T15 cell is obtained from membrane and whole-channel conductances, which would be increased if the lower conductance in 5 mmol/l K+ 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 subjects. During euglycemic hyperinsulinemia (n = 7) at 40 μu/l, m-LPLA decreased from 30 μU/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-triglycerides (TG) by 47%, LDL-cholesterol (C) by 5% and HDL-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 activation of IRK, insulin receptor kinase (IRK).

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


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 hour 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 ± 0.56/CVmin (r = 0.862, p < 0.001),
3) CVresp = 0.50 ± 0.95/CVmax (r = 0.071, p < 0.001).

Since the slope in (1) was steeper than expected by the study design it 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 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. Isolated rat adipocytes were preincubated for 30 min at 37°C with 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 [32P]-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 prereated with isoproterenol, the insulin concentrations of insulin needed to activate IRK were 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, respectively. In contrast, no alteration in [3H]-insulin binding to cells preincubated with isoproterenol was observed (0.29 ± 0.05% and 0.28 ± 0.04% per 10⁷ 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 assessed whether the expression of class II molecules, i.e. IA antigens, is affected 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 Ia antigens. Monoclonal antibody-determined ICs were 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 (CCK₈) 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 [³H]arachidonic acid for 90 min glucose decreased the incorporation of label into phosphoinositols and phosphatidylserines (P1-PS), phosphatidylethanolamine (PE) and phosphatidylglycerol (PG) in a dose-dependent manner. 10 nmol/l CCK₈ increased this glucose effect with respect to PC, PE and PG. In myo-[³H]inositol prelabelled islets glucose in a dose-dependent manner increased inositol-1,4,5-triphosphate (IP3) without affecting inositol phosphate (IP1) and inositol-1,4-bisphosphate (IP2). 10 nmol/l CCK₈ dramatically increased IP3 and IP1, and marginally IP2, 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. CCK₈ concomitantly decreased the sum of inositolphosphates such as phosphatidylinositol 4,5-bisphosphate and phosphatidylinositol 4-phosphate. The data indicate a lower PC, PE and PG labelling and a higher emergence of inositol phosphates probably from polyphosphoinositides in rat pancreatic islets induced by CCK₈; this shift may be involved in the sensitising effect of islets to glucose-mediated insulin release by CCK₈.