lottery gambling and accident insurance. After reviewing the patients' answers, however, it became clear that some were illogical, which suggested that these patients did not understand the context of the questions, the hypothetical economical situations, or even the instructions, probably because of lower literacy skills. Thus, we labeled these patients as the unreasonable (UR) group (n = 81), and the patients who provided appropriate answers, even if extremely risk averse or risk loving, were labeled as the reasonable (R) group (n = 195). The prevalence of UR answers generally increased with age (<50 y, 16%; 50-64 y, 10%; 65-74 y, 37%; ≥75 y, 64%) ($p < 0.0001$). After age adjustment, there was a significant correlation between the UR answers and educational attainment in both sexes. The prevalence of UR answers was significantly higher in females (38.6%) than in males (24%) ($p < 0.01$), which may be partly because the average number of educational years was lower for females than for males (males, 13.8 y; females, 12.9 y; $p < 0.05$), but both averages are very high among all countries. The prevalence of retinopathy was significantly higher in the UR than the R group in males ($p < 0.05$), but not in females. Job and economic status were not associated with prevalence of retinopathy. These results suggest that effects of literacy skills on progression of diabetic retinopathy may be sex dependent. Although the mechanism underlying this finding is unknown, sex may be an important biological factor beyond socioeconomic status in highly educated high-income countries.

Steroid Hormones and Receptors

STEROID AND NUCLEAR RECEPTORS

Androgen Receptor Phosphorylated at Serine 815 in Mouse and Human Prostates

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SUN-LB134

Androgen receptor (AR) regulates male sexual development and maintenance. AR forms a homodimer in the cytoplasm and monomerizes following hormonal activation, translocating to the nucleus in Cos-1 cells (Shizu et al. *Scientific reports*. 2019). Utilizing Ser815 of AR, the conserved phosphorylation residue within the ligand binding domains of steroid hormone receptors (NR3C), whether and how this phosphorylation regulates AR functions was investigated. While, like AR WT, a phosphomimic AR S815D mutant formed a homodimer in the cytoplasm, unlike the WT, this mutant remained as a homodimer in the cytoplasm even after hormone treatment. Apparently, Ser815 phosphorylation disabled AR's capability to monomerize and nuclear translocate in Cos-1 cells. A phospho-Ser815 peptide antibody was used to detect phosphorylation of endogenous AR in mouse as well as human prostates. Immunohistochemistry showed phosphorylation present in both the cytoplasm and nucleus. Mouse prostates were cell fractionated in cell membrane, mitochondria, endoplasmic reticulum (ER) and cytosolic fractions for subsequent Western blot analysis. While AR was found in all of these fractions, phosphorylated AR was only detected in the ER and cytosolic fractions. A cDNA microarray analysis of PC-3 cells with ectopic expression of AR S815D suggested that phosphorylated AR may regulate ER stress.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Insulin Resistance in Type 1 Diabetes Managed With Metformin (INTIMET): Rationale and Study Design of a Randomised Placebo-Controlled Trial

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Background: Insulin resistance is an under-recognised cardiovascular risk factor in type 1 diabetes (T1D). Individuals with T1D exhibit insulin resistance relative to those without diabetes. In T1D, tissue-specific insulin resistance (muscle, hepatic, adipose) is likely to partly drive increased cardiovascular risk. Adjunctive metformin improves muscle insulin sensitivity in T1D adolescents, but factors that predict responsiveness remain unknown.**Objective**: To report the rationale and design of the INTIMET study, a double-blind randomised, placebo-controlled trial of metformin in T1D.**Methods:** Forty adults aged 20-50 years with T1D, and 20 age- gender- and BMI- matched non-diabetic controls will be studied. T1D inclusion criteria are diagnosis > 10 years, HbA1c 9.5% and fasting C-peptide < 0.3nmol/L. Liver and muscle insulin sensitivity will be determined by the 2-stage hyperinsulinemic (20 and 60 mUm^2)-euglycemic (5.5 mmol/L) clamp method with deuterated glucose. Subjects with T1D will be randomised to metformin extended-release 1500mg/d or matched placebo for 26 weeks. The primary endpoint is the change in hepatic insulin sensitivity, measured by suppression of endogenous glucose production (EGP) with the low-dose insulin clamp. Secondary endpoints include change in muscle and adipose tissue insulin sensitivity, arterial stiffness, HbA1c, glucose variability, frequency of hypoglycemia, insulin dose, anthropometry, body composition, lipid profile, liver fat and stiffness. **Conclusion**: The INTIMET study will quantify muscle, liver and adipose insulin-resistance in T1D, determine whether metformin is effective in improving insulin resistance in T1D and identify factors that predict metformin-responsiveness. The trial is registered (Australian New Zealand Clinical Trial Registry, ACTRN12619001440112) and is actively recruiting in Sydney, Australia.

Adrenal

ADRENAL - TUMORS

Clinical Features, Treatment and Prognosis of Primary Bilateral Macronodular Adrenal Hyperplasia Compared With Unilateral Adrenal Cortisol-Secreting Adenoma: Analysis of 46 Chinese Cases

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