Christchurch Medical Research Society

Scientific Meeting

Friday 26 July 2002

12:00 – 1:30 pm in the Rolleston Lecture Theatre

12:00 LUNCH IN THE GROUND FLOOR FOYER

12:30 ORAL PRESENTATIONS

12:30 Visuoperceptual and visuomotor deficits in developmental stutterers
Richard D. Jones, Amanda J. White, Kim H. C. Lawson, Tim J. Anderson

12:45 Ghrelin constricts coronary arteries in an isolated perfused heart model: Role of L-type Ca^{2+} Channels and PK-C
Chris J. Pemberton, Heikki Tokola, Juhani Pontinen, Antti Ola, Olli Vuolteenaho, Heikki Ruskoaho

1:00 Sedative drug administration patterns in surviving and non-surviving critically ill patients
A D Rudge*, G Shaw, J G Chase

1:15 Postprandial Resistance-Vessel Function is Unaltered by Improved Glycaemic Control in Postmenopausal Women with Type 2 Diabetes
Christopher H. Strey*, Joanna M. Young, Brett I. Shand, Christopher M. Florkowski, Russell S. Scott

* Contestants for the CMRS Young Researcher Prize

Visuoperceptual and visuomotor deficits in developmental stutterers

Richard D. Jones[1,2], **Amanda J. White**[3], **Kim H. C. Lawson**[4], **Tim J. Anderson** [2,4]

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Although the precise cause of stuttering is unknown, there is strong evidence for it being a neuromotor disorder characterised by an abnormality of higher control, encompassing not only speech but other motor systems, and an overactive dopamine system. The aim of this study was to look for the presence of non-speech/language deficits – in particular, visuomotor and visuoperceptual deficits – in persons who stutter.

Twelve moderate to severe developmental stutterers were compared with a group of fluent speakers, matched for age and sex, on a range of computerized sensory-motor tasks. These tasks covered various aspects of visuoperceptual function – acuity, static perception, and dynamic perception – and visuomotor function – ballistic movement, dynamic steadiness, and several types of tracking. A novel technique was used to remove the visuospatial component from tracking performance (Jones et al., *IEEE Trans Biomed Eng* 1996;43:1001-1010).

Stutterers had slower reaction times (11%, $p = 0.014$) and less accurate random tracking (preview: 16%, $p = 0.068$; non-preview: 16%, $p = 0.030$). They also exhibited impaired dynamic visual perception (44%, $p = 0.014$), and minimally impaired static visual perception (3%, $p = 0.054$). Severity of stuttering correlated with reaction time ($r = 0.58$, $p < 0.05$) and dynamic perception ($r = 0.79$, $p < 0.01$). Removal of the visuoperceptual component from tracking performance indicated that the impaired tracking in the stutterers was predominantly due to reduced dynamic perception.

This is the first study to demonstrate the presence of non-linguistic visuoperceptual and manual tracking deficits in people with moderate to severe stuttering. The finding of subtle visuomotor and visuoperceptual deficits supports a neurogenic aetiology for stuttering and is compatible with recent evidence for an overactive dopamine system in stutterers.

Ghrelin constricts coronary arteries in an isolated perfused heart model: Role of L-type Ca^{2+} Channels and PK-C.

Chris J. Pemberton[1], Heikki Tokola[2], Juhani Pontinen[2], Antti Ola[2], Olli Vuolteenaho[3], Heikki Ruskoaho[2].

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Ghrelin, discovered in 1999, is a novel Growth Hormone (GH)-stimulating peptide, which is primarily secreted from the stomach and is a potent endogenous regulator of energy balance and feeding. However, recent reports in humans have suggested that ghrelin also possesses cardiovascular actions, where it decreased mean arterial pressures in normotensive subjects. Added to this, the growth hormone secretagogue receptor (GHS-R), through which ghrelin acts, has been identified in cardiac endothelial cells. However, direct cardiac actions of ghrelin have not been reported. Accordingly, we administered incremental infusions of ghrelin (0.1-10nM) to isolated, perfused rat hearts and neonatal cardiomyocyte cultures to determine its effects upon cardiac contractility and natriuretic peptide secretion and gene expression. At the dose of 1nM, ghrelin increased coronary perfusion pressure (44±9%(SD), $P<0.01$) over one hour and this could be blocked by Diltiazem (Dil, L-type Ca^{2+} channel antagonist) and Bisindolylmaleimide (Bis, PK-C antagonist). The negative inotropic effect of Dil (-30±3%, $P<0.01$) was abolished during co-infusion with ghrelin. Dil and Bis induced decreases in ANP secretion in isolated hearts were not altered by ghrelin co-infusion. Finally, administration of ghrelin to cardiomyocytes in culture for up to 48 hours did not elicit changes in ANP or BNP peptide secretion or gene expression. Thus, in isolated perfused heart preparations, ghrelin has a unique, slow acting coronary vasoconstrictor action that is partially dependent on Ca^{2+} and PK-C, and appears to have a role in Ca^{2+} gain with respect to cardiac contractility, but no effect on cardiac natriuretic peptide secretion/gene expression.

Sedative drug administration patterns in surviving and non-surviving critically ill patients.

A D Rudge[1], G Shaw[2], J G Chase[1]

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The effective delivery of sedation is a 'core activity' in any intensive care unit, yet it is perhaps one of the most arbitrarily applied therapies. Insufficient sedation leads to agitation, while over-sedation is potentially damaging, increases length of stay and is expensive. A semi-automated drug delivery algorithm using sedation-agitation scales was implemented to minimise patient sedation dosage while minimising agitation. The algorithm adjusts the background infusion rate based on the total average drug delivery (infusion and boluses combined) during the previous four hours, reducing the background rate in the absence of agitation. Fixed ratio morphine (1mg/mL) and midazolam (0.5mg/mL) solution was used in the study. Forty-eight days of data from 10 patients were collected and grouped into surviving and non-surviving patients. Data averaging and frequency analysis methods were employed to identify patterns in the drug administration profiles. Notable differences in drug administration profiles between survivors and non-survivors are evident. On average survivors receive clusters of smaller (0.8 mL/h) extra boluses 4-12 times daily, whereas non-survivors receive clusters of larger (1.6 mL/h) extra boluses 1-4 times each day. Each cluster may occur over 1-4 hours for survivors indicating lighter more uniform control input, resulting in a relatively flat background sedation infusion rate of approximately 1.2 mL/h. Non-survivors exhibit abrupt increases in infusion rate and experience large, daily agitation-sedation cycles indicating heavier less effective control effort. These results provide a better understanding of agitation and sedation in critically ill patients.

Postprandial Resistance-Vessel Function is Unaltered by Improved Glycaemic Control in Postmenopausal Women with Type 2 Diabetes

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Type 2 diabetes is associated with atherogenic metabolic disturbances in the postprandial state. Atherosclerosis is preceded by endothelial dysfunction. The forearm blood flow (FBF) response to a meal is used to evaluate postprandial endothelial dysfunction. We hypothesized that improved glycaemic control enhances endothelial function in resistance-vessels in the postprandial state.

FBF was measured with venous occlusion plethysmography before and 3h after a meal (660kcal, 55% fat) in 19 type 2 diabetic (DM) and 10 healthy postmenopausal women (Control) during intra-arterial infusion of 0, 20 (A20), or 40 (A40) μg/min acetylcholine. Measurements were repeated in the DM group after optimising glycaemic control over 3 months. Lipoproteins and glycaemic indices were obtained immediately before all FBF measurements.

Postprandial triglycerides, insulin and glucose were higher in the DM group than in the control group ($p<0.01$). In the DM group HbA1c was decreased by 0.96±0.26% ($p<0.01$) and postprandial glucose by 2.37±1.07mmol/L ($p<0.05$) without a concomitant increase in insulin. In the absence of acetylcholine FBF did not differ between the study groups, irrespective of the prandial state. During acetylcholine infusion FBF was lower in the DM group before and after the meal ($p<0.05$). The meal increased FBF in the DM and the Control group in the absence of and during acetylcholine infusion ($p<0.05$, NS for A40 in Controls). This meal-induced increase in FBF did not differ between the study groups and did not correlate with postprandial metabolic changes. Improved glycaemic control was associated with higher FBF during A40 infusion (pre-meal $p=0.064$, post-meal $p<0.05$). Better glycaemic control did not significantly alter the meal-induced increase in FBF.

A high-fat meal does not impair endothelium-dependent FBF in postmenopausal women. The FBF response to a meal is not altered by the presence of diabetes or by improved endothelial function after 3 months of better glycaemic control, suggesting that the meal-induced increase in FBF is independent of the functional state of the endothelium.