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ACUTE ATRIAL DILATATION INCREASES HETEROGENEITY OF CONDUCTION IN THE LANGENDORFF PERFUSED RABBIT HEART.

Eijsbouts SCM, Zarse M, Allessie MA.

Atrial Fibrillation (AF) is often associated with atrial dilatation (AD). We tested the hypothesis that AD increases spatial heterogeneity in conduction in the Langendorff perfused rabbit heart (n=6), by high density mapping (240 electrodes, interelectrode distance 350-700 μm). The mapping probe covering an area of 7 × 7 mm was positioned on the free wall of the right atrium with one edge parallel on the crista terminalis (CT). Right atrial pressure (RAP, cm H_2O) was increased by raising the outflow of the cannulated right atrial orifices from 4 cm, during control to 10 and 16 cm, respectively. The right atrium was paced at 3 different sites (cranial part of the CT, superior and inferior parts of the free wall) at pacing intervals of 240, 140 and 100 ms. The mean local conduction velocity (CV) was calculated in each of 190 quadripoles of electrodes 700 μm apart. Increase in RAP from 4 to respectively 10 and 16 cm H_2O stretched the surface of the free atrial wall by 45±11 % and 54±13 %. In the table below the mean values of CV, % of slow conduction (10-20 cm/s) and % of conduction block (< 10 cm/s) during pacing from three different directions are given. Statistical significance refers to values during RAP of 4 cm H_2O at the same pacing interval ($^{+}p<0.05$, $^{*}p,0.01$, $^{\#}p,0.001$).

	Mean local CV(cm/s)			% Slow Conduction			% Conduction Block		
RAP	4	10	16	4	10	16	4	10	16
240 ms	53±7	49±7	41±10$^{\#}$	16±9	19±7	26±9*	3±3	7±8^{+}	15±17*
140 ms	52±4	44±12^{+}	38±9$^{\#}$	16±7	25±10^{+}	27±8*	2±4	9±11^{+}	19±18*
100 ms	45±4	39±8^{+}	33±7$^{\#}$	22±6	26±11	31±8*	7±9	15±12	20±16*

Both rapid pacing and atrial dilatation depress mean local CV from 53±7 cm/s during slow pacing at a RAP of 4 cm H_2O, to 33±7 cm/s during rapid pacing and a RAP of 16 cm H_2O. The incidence of areas of slow conduction and conduction block markedly increased from 16±9 to 31±8 % and from 3±3 to 20±16 %, respectively ($p<0.001$). This increased spatial heterogeneity in conduction may contribute to perpetuation of AF in dilated atria.

Department of Physiology, Cardiovascular Research Institute Maastricht (CARIM) Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

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DIFFERENCES IN PHASE 1 REPOLARIZATION IN ISOLATED SHEEP PURKINJE CELLS: ROLE OF TRANSIENT OUTWARD CURRENT AND CALCIUM CURRENT.

A.O. Verkerk, A.C.G. van Ginneken, M.W. Veldkamp, L.N. Bouman.

Membrane potentials and currents of single cells, enzymatically isolated from free-running Purkinje fibres of the sheep, were studied using the amphotericin perforated patch clamp technique. Cells were continuously superfused with HEPES buffered Tyrode's solution (35-37 °C). Action potentials (AP's) were elicited by 2 ms current pulses of 1.5 x threshold at a frequency of 1 Hz. We observed two different AP configurations. The first type had a large phase 1 repolarization and a relatively negative plateau. The second had no or small phase 1 repolarization and a more positive plateau. AP durations at 20 and 90% of repolarization were significantly longer in cells without phase 1 repolarization. The calcium current (I_{Ca}) and the quasi steady state current ($I_{steady\ state}$) were measured during 500 ms test pulses at various potentials from a holding potential of −40 mV in presence of 2 mM 4-aminopyridine (4AP). $I_{steady\ state}$ did not differ significantly for the two types but I_{Ca} was significantly smaller in cells showing AP's with large phase 1 repolarization. The 4-aminopyridine sensitive transient outward current (I_{to1}) was measured during 500 ms depolarizing voltage steps from a holding potential of −80 mV in the presence of 1 mM $CdCl_2$. I_{to1} was significantly larger in cells with AP's showing large phase 1 repolarization. To test whether the differences in AP's and membrane currents are caused by the Isolation method, AP's were also measured in intact free-running Purkinje fibres using micro-electrodes. Like in isolated cells, the same two types of AP's were found in intact Purkinje fibres. These results show that the observed differences in AP configuration in sheep Purkinje cells are caused by a combination of differences in I_{to1} and I_{Ca} density.

Department of Physiology, University of Amsterdam, Meibergdreef 15, 1105 AZ Amsterdam, the Netherlands.

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AN ANIMAL MODEL TO INVESTIGATE CEREBRAL METABOLISM OF FETAL LAMBS IN UTERO DURING HYPOXIA BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY.

A.M. Van Cappellen van Walsum, H.W. Jongsma, A. Heerschap, J.G. Nijhuis, J. Crevels, R. Nijland, J. Van Asten, B. Oeseburg.

In this pilot study we developed a method to investigate the relation between fetal cerebral metabolism and arterial oxygen saturation (SaO_2). Nuclear magnetic resonance spectroscopy (NMRS) of the fetal brain provided "in vivo" simultaneous sequential observations of cerebral metabolites in the same animal. Problems arising from measurements in a NMR setting like fitting the ewe in the bore hole, ventilatory support and fixation of the fetal head to avoid movement artefacts had to be solved.

Under general anesthesia pregnant ewes of the Dutch Texel breed were operated between 120 and 128 days of gestation (term 147 days). The fetal head was delivered by hysterotomy and fixed. The axillary artery was cannulated for measurements of SaO_2, pH and base excess (BE). A radiofrequency surface coil was located on the vertex of the fetal head to receive the NMR signal. The ewe was ventilated by a system with 12m long tubing inside a 1.5T Siemens magnetic resonance system. After baseline measurements the fetal SaO_2 was gradually reduced by lowering inspired oxygen of the ewe.

The long tubing caused a delayed gas exchange. Fetal hypoxia (SaO_2=10%) allowed a pH of 7.10 and BE of -15.0 to be achieved. The fetal body moved as a result of the maternal ventilation, but the fetal head stayed still. Cerebral spectra were obtained showing signals assigned to compounds such as inositol, choline, creatine, N-acetylaspartate and lactate.

NMRS of fetal lamb brain in utero during hypoxia is feasible and may serve as an animal model to investigate fetal cerebral metabolism in relation to SaO_2 and other circulatory parameters.

Department of Obstetrics and Gynecology and Physiology and Diagnostic Radiology, Faculty of Medical Sciences, P.O. Box 9101, 6500 HB Nijmegen.

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THE ASSESSMENT OF GASTRIC EMPTYING OF LIQUIDS DURING EXERCISE USING A 13C-ACETATE BREATH TEST.

M.A. van Nieuwenhoven[1], J. Senden[1], A.J.M. Wagenmakers[1], F. Brouns[1], R-J.M. Brummer[2].

Introduction: The standard method for measuring gastric emptying of liquids during physical exercise is the invasive double sampling aspiration technique. Scintigraphy is not possible. The aim of the study was to compare a non-invasive breath test with the double sampling technique for the determination of gastric emptying of liquids during physical exercise.

Methods: After an overnight fast, 9 healthy well-trained male subjects were studied twice at rest (Re), and twice during physical exercise (Ex) on a cycle ergometer at 60% of their Wmax. A solution of 500 ml containing either 4.5% or 9.0% carbohydrate (CHO) and 50 mg [1-13C]-acetate (Ac) at Re, and 150 mg of Ac during Ex, and 7.5 mg phenol red [Re4.5%, Re9.0%, Ex4.5% and Ex9.0%] was administered via a naso-gastric tube. Gastric aspirates and breath samples were collected at regular intervals. Gastric half emptying time (T1/2 GE) was determined from phenol red concentration in the gastric aspirates. 13C-enrichment of the breath samples was measured using Isotope Ratio Mass Spectrometry (Finnigan MAT 252). Time to peak 13C-enrichment (13C-TTP) was determined by fitting the data to an exponential function, and was regarded as the parameter of gastric emptying. VCO2 was continuously monitored by indirect calorimetry.

Results: Values are given in minutes (mean±sem). Correlations were calculated between 13C-TTP and T1/2 GE, and are displayed in the table. Both tests showed that the 9.0% solutions emptied slower than the 4.5% solution. No difference in T1/2 GE was found between Ex and Re, but the 13C-TTP was reached significantly earlier during Ex than at Re for both solutions ($p<0.05$). During exercise the rate of metabolism and CO2 washout is increased. This explains the difference between Ex and Re. During both Ex and Re the VCO2 was constant in time.

	T1/2 GE	13C-TTP	corr.	p (*=signif.)
Re4.5%, 50 mg Ac	16.9±1.7	30.4±1.9	0.71	0.03 *
Re9.0%, 50 mg Ac	23.6±2.7	35.4±3.1	0.78	0.01 *
Ex4.5%,150 mg Ac	14.2±2.3	20.2±2.2	0.87	0.0006 *
Ex9.0%,150 mg Ac	21.9±3.0	24.5±2.3	0.70	0.033 *

Conclusion: The 13C-acetate breath test can be used to determine the relative differences in the gastric emptying rate of liquids during physical exercise.

Depts. of [1]Human Biology and [2]Gastroenterology, Maastricht University, P.O. box 616, 6200 MD Maastricht, The Netherlands.