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Session I. Circulation and cellular and molecular physiology

Physiological cardiac hypertrophy and gene expression of β adrenergic and M_2 muscarinic receptors. J. Barbier, J. Marchais, F. Rannou-Bekono, F. Carré (Laboratoire de Physiologie, Université de Rennes 2, Av. C. Tillon, 35044 Rennes Cedex, France).

Endurance training induces cardiovascular adaptations. Alterations in the expression of β adrenoreceptors (β AR) and in M_2 muscarinic receptors (M AchR) have been suggested to be involved in these processes but their understanding is incomplete. The objective of this work was to assess if adaptations linked to endurance training are associated with modifications in mRNA abundance and/or protein levels of different β-AR subtypes and M_2 AchR. At the end of an 8 weeks treadmill protocol, cardiac parameters were evaluated by an electrocardiographic analysis. We measured β AR and M_2 AchR mRNA level (by real-time RT-PCR) and protein density (by western blot). A physiological cardiac hypertrophy (+11%), a bradycardia ($P < 0.01$) and an increased diastolic function ($P < 0.01$) were observed in trained rats. The β_3 AR mRNA level remained unchanged in trained as compared to sedentary rats; by contrast, the β_3 AR protein density increased (+54%; $P < 0.05$). There was no change in β_1 AR mRNA level associated to a non-significant trend towards a decrease of β_1 AR protein level (–26%; $P = 0.07$) in trained rats. These results also suggest a post-translational regulation of β_1 AR and β_3 AR gene expression. For β_2 AR and M_2 AchR, there was no change neither in mRNA level nor in protein density. This study shows that adrenergic and muscarinic systems are differentially regulated following training when using results on mRNA and protein expression of these cardiac receptors. Moreover, morphological and cellular adaptations related to training seem, to some extent, to be similar as noted in hearts affected by diabetes or in heart failure. However, the modifications induced by physical training, are involved in beneficial cardiovascular modulations.

C-Protein phosphorylation by PKA modulates cardiac contractile activity. O. Cazorla, S. Szilagyi, N. Vignier, G. Vassort, L. Carrier, A. Lacampagne (Inserm U-637, CHU Arnaud de Villeneuve, 34295 Montpellier, France).

β-adrenergic stimulation modulates cardiac contractility through protein kinase A (PKA), which phosphorylates several cellular proteins, such as cardiac troponin I (cTnI) and cardiac C-protein (cMyBP-C). The relative contributions of cTnI and cMyBP-C to the regulation of myofilament Ca^{2+} sensitivity are still controversial because of difficulty in targeting phosphorylation to specific proteins. In the present work, we studied the PKA effect on myofilament Ca^{2+} sensitivity of the left ventricular skinned myocytes isolated from wild type mice (WT) and cMyBP-C deficient mice (KO) at two sarcomere lengths (SL: 1.9 and 2.3 μm). Without PKA stimulation and at the shorter SL, Ca^{2+} sensitivity was higher in KO than in WT. No difference in passive tension or maximal active tension was observed. PKA stimulation induced a desensitisation to Ca^{2+} of WT myofilaments at both SL. It had almost no effect on KO myofilaments even though cTnI was phosphorylated to a similar level in both WT and KO hearts. These observations were similar whether obtained on 5-week old mice that showed a light cardiac hypertrophy or on 55-week old mice with clear signs of cardiac insufficiency, indicating that these observations do not depend upon the cardiac physiopathological state. The results suggest that cMyBP-C contributes to the regulation of cardiac contraction during β-adrenergic stimulation and its phosphorylation, as well as that of TnI, is required for the decrease in Ca^{2+} sensitivity reported under these conditions.

Effect of different frequencies of exercise on endothelium-dependent vasodilation in rat thoracic aorta. E. Heylen, F. Guerrero, J.

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The effects of exercise training frequency on endothelial function were investigated by measuring isometric tension in rings of the thoracic aorta isolated from male Wistar rats submitted to different treadmill training protocols. Vascular responses to ACh (10^{-9}–10^{-4} M) and SNP (2.10^{-8} M) were examined in rings precontracted with PE (10^{-7} M). Dose-response curves to ACh (10^{-8} to 10^{-5} M) were also performed in the presence of 5.10^{-5} M of L-NAME, 10^{-5} M of indomethacine or 10^{-6} M TEA. In 3 groups, rats were submitted to an 8-week treadmill training protocol (15 m.min^{-1}, 15% incline, 60 min.day^{-1}). The animals in these exercise groups ran either 1 day.week^{-1} (Ex1), 3 day.week^{-1} (Ex3), or 5 day.week^{-1} (Ex5). A fourth group was composed of age matched sedentary animals, [restricted to cage activity during 8 weeks (Sed)]. The aimals in the control group (Control) were of the same age as those in the Ex and Sed groups before the 8 week protocol. SNP-induced vasodilation was neither modified by aging (Sed group) nor by chronic exercise. The maximal response to ACh was not different between groups, while EC_{50} values were inversely correlated with the frequency of training. In Young as well as Ex3 and Ex5 rats, responses to 10^{-6} and 10^{-5} M ACh concentrations were significantly inhibited by L-NAME, indomethacine and TEA. In Sed animals, 10^{-5} M of ACh-induced vasodilation only was inhibited by L-NAME. These results indicate that (i): the decrease in endothelium sensibility to ACh with ageing is due to impaired eNOS, COX and EDHF pathways and (ii): this effect is totally reversed by a training frequency of 3 or more bouts weekly.

Inducible production of erythropoietin using intramuscular injection of block copolymer/DNA formulation. B. Pitard, P. Richard, L. Desigaux, C. Gourden (Institut du Thorax, Inserm U533, Faculté de Médecine, 44000 Nantes, France).

We have previously shown that intramuscular injection of plasmid DNA formulated with a non ionic amphiphile synthetic vector [poly(ethyleneoxide)$_{13}$-poly(propyleneoxide)$_{30}$-poly(ethyleneoxide)$_{13}$ block copolymer; PE6400] increases reporter gene expression compared to naked DNA. We investigated this simple non-viral formulation for production of secreted proteins from the mouse skeletal muscle. Plasmids encoding either constitutive human secreted alkaline phosphatase or murine erythropoietin inducible via a Tet-on system, were formulated with PE6400 and intramuscularly injected into the mouse tibial anterior muscle. PE6400/DNA formulation led to an increased amount of recombinant alkaline phosphatase secreted from skeletal muscle as compared to naked DNA. In the presence of doxycycline, a single injection of 10 μg plasmid encoding inducible murine erythropoietin formulated with PE6400 significantly increased the hematocrit, whereas the same amount of DNA in the absence of PE6400 had no effect. The increase in the hematocrit was stable for 42 days. The tetracycline-inducible promoter permitted pharmacological control of the hematocrit level after DNA intramuscular injection. However, 4 months post-injection, the hematocrit returned to its pre-injection value, even in the presence of doxycycline. This phenomenon was likely caused by an immune response against the tetracycline-activated transcription factor. Intramuscular injection of plasmid DNA formulated with PE6400 provides an efficient and simple method for secretion and production of non-muscle proteins.

Opposite alterations of vascular global β-adrenergic and β_3-adrenergic response early and late stages of congestive heart failure in rats. C. Sèze, A. Bammert, G. Toumaniantz, L. Audigane, S. Serpillon, C. Gauthier (Institut du Thorax, Inserm U533, Faculté de Médecine 44035 Nantes, France).

Congestive Heart Failure (CHF) is characterised by cardiac function and structure alterations, but also by an increase in peripheral vascular resistance. This study investigated the vascular β-AR remodelling in a rat CHF model produced by ligating the left coronary artery. Two or 12 weeks after infarction (2W or 12W),

the thoracic aortae rings of rats were placed in organ baths to measure isotonic contraction. Three groups of rats were designed: SHAM (thoracotomy without ligature), compensated CHF (PED >15 mmHG: ICC) and overt CHF (CHF and pleural effusion: ICD). The rings were contracted with phenylephrine (α_1-AR agonist) and concentration-relaxation curves to isoproterenol (ISO, specific β-AR agonist) and SR 58611A (SR, β_3-AR agonist) were performed. At an early stage of CHF (2W), a maximal ISO response was potentialised (ICC 85 ± 3% (n = 6), SHAM 78 ± 2% (n = 8), $P < 0.05$) whereas at 12W it was blunted (ICD 42 ± 3% (n = 6), ICC 48 ± 2% (n = 6), $P < 0.05$) versus SHAM (57 ± 4% (n = 8)). Surprisingly, maximal SR response was decreased at 2W in ICC (67 ± 8% (n = 6), $P < 0.01$) compared to SHAM (81 ± 2% (n = 7)), but was restored at 12W (ICD 87 ± 3% (n = 7), ICC 89 ± 3% (n = 6), SHAM 87 ± 1% (n = 7)). At 2W, the SR-induced relaxation was only significantly blunted in SHAM by pretreatment with 100 μM of L-NMMA (NO synthase inhibitor) suggesting the recruitment of another signalling pathway in the β_3-AR response in ICC (Emax: SHAM 55 ± 6% (n = 4), ICC 61 ± 6% (n = 6)). In conclusion, we demonstrated that vascular global β-AR and β_3-AR -induced relaxation were modified at early and late stages of CHF in an opposite manner. Additional experiments were clearly needed to determine the cellular mechanisms involved in these alterations.

Heart rate variability in mice: limits and difficulties. J. Thireau, B.L. Zhang, D. Poisson, D. Mohty, P. Cosnay, D. Babuty (UMR-CNRS 6542, Physiologie des cellules cardiaques et vasculaires, Université François-Rabelais, 37200 Tours, France).

The study of heart rate variability (HRV) is useful for the evaluation of the rhythmic prognosis of cardiac diseases and the drug effects on cardiac rhythm and neurovegetative system. For several years, this method used in Humans has been applied in laboratory animals. However, it is unsuitable because of the high cardiac frequency in mice (600 bpm) and justifies to be modified. The aim of this work was to estimate the reliability of HRV analysis in mice by using the ECG-auto 1.5 software (EMKA-Technologies). Electrocardiograms were recorded by telemetric techniques (DSI). HRV analysis assumes sinus rhythm. Thus, the artifacts and arrhythmia had to be eliminated. In the time domain, we retained the RR intervals between the mean RR interval ± 2 SD, over long periods (2 × 12 h) and the parasympathetic marker was adapted to the cardiac frequency of mice (pNN 6 ms). In the frequency domain, the analysis with a Fast Fourier transform and over long periods (advised for man) was inadequate because only one ULF band was individualised which is due to the non stationarity of the signal. So we selected several short stable periods of three minutes distributed over 24 h. The reproducibility of the results of HRV were dependent on the method of analysis: in the time domain, the short period (from 30 to 60 min) of analysis was not reproducible but, in the frequency domain the results obtained from repeated short period recordings were reproducible. In conclusion, HRV analysis in mice is possible in the time and frequency domains. This analysis was expensive at the time and requires cautiousness for the result interpretation.

Session II. Digestion, nutrition, metabolism and thermoregulation

Docosahexaenoic acid modulates intracellular calcium concentrations via activation of PKCγ and PKCδ in U937 cells. V. Aires, A. Hichami, R. Filomenko, A. Bettaieb, N.A. Khan (Département de physiologie, UPRES Lipides et Nutrition, Université de Bourgogne, 6 Bd Gabriel, Dijon, France).

Stimulation of plasma membrane receptors linked to phospholipase C and the subsequent production of the second messengers like diacylglycerol (DAG) and inositol-1,4,5-triphosphate (IP_3) is a signalling pathway of fundamental importance in eukaryotic cells. Downstream signalling involves mobilisation of Ca^{2+} from intracellular stores (mainly endoplasmic reticulum pool) and Ca^{2+} influx

through the opening of store-operated Ca^{2+} (SOC) channels. Several studies have shown that protein kinase C (PKC) modulates various ion channel activities including SOC. The present study was conducted in monocytic leukemia U937 cells to investigate the effects of docosahexaenoic acid (DHA), an n-3 polyunsaturated fatty acid, on calcium signalling and to determine the implication of PKC in this pathway. Fura 2 fluorescence ratiometry showed that DHA stimulated SOC influx via the opening of calcium release-activated calcium (CRAC) channels. Pretreatment of cells with the PKC inhibitors (GF109203X, Calphostin C and Chelerythrin) significantly inhibited the DHA-induced calcium peak. To gain insight into the specific isoform(s) of PKC involved in DHA-induced response, we examined the effects of isoform-specific inhibitors. Incubation of cells with HBDDE (PKCα and γ inhibitor) and Rottlerin (PKCδ inhibitor) significantly diminished DHA-induced rise in $[Ca^{2+}]_i$. However, Hispidin (PKCβI/II inhibitor) and Gö-6976 (PKCα and βI inhibitor) failed to affect a DHA-evoked calcium peak. In vitro PKC activity assays also revealved a 2-fold increase in PKCγ and δ activities following stimulation by DHA. Together these results suggest that DHA-induced calcium influx occurs via the opening of CRAC channels and activation of PKCγ and δ in U937 cells.

Modulation of gestational diabetes and macrosomia by n-3 fatty acids. A. Hichami, N.A. Khan (Département de Physiologie, UPRES Lipides et Nutrition, Université de Bourgogne, Dijon, France).

Maternal diabetes during pregnancy is an important risk factor for foetal over nutrition leading to fœtal obesity and hyperinsulinemea. Foetal hyperinsulinemia is associated with the development of glucose intolerance, obesity and diabetes during childhood and adulthood. We used an animal model in which mild hyperglycemia in pregnant rats resulted in obese hyperglycaemic and hyperinsulinemic offspring. Diabetic mothers and their obese offspring have an impairment of lipid metabolism and an abnormal T-cell functioning. Since n-3 polyinsaturated fatty acids (n-3 PUFA) are known for their immunosuppressive effects and may exert beneficial effects on serum lipids, we investigated the effects of diet containing these n-3 PUFA on the time course of changes in lipoprotein metabolism and T-cell activation in diabetic mothers during pregnancy and their macrosomic offspring during childhood and adulthood. We observed that the n-3 PUFA diet diminished glycaemia of diabetic rats but did not affect body weight and glycaemia of macrosomic pups. Furthermore, compared with control rats, diabetic rats and their obese offspring showed a significant elevation in liver, and serum triglyceride and cholesterol concentrations mostly reflected in VLDL and LDL-HDL1 fractions. We also observed that the n-3 PUFA diet restored T cell proliferation which was decreased in both pregnant rats and their obese offspring. Diabetes also decreased the ratio of IL4/IL2 mRNA in spleen T cells, whereas the n-3 PUFA diet increased this ratio in the favour of T-cell differentiation toward the Th2 phenotype. Hence, we can consider the use of the n-3 PUFA diet in medical counselling

Control of food intake by fatty acid oxidation in a rat model resistant to diet-induced obesity (Lou/C). G. Lacraz, K. Couturier, R. Favier, X. Leverve (Inserm E-0221, Bioénergétique Fondamentale et Appliquée, Université Joseph Fourier, Grenoble, France).

Mitochondrial fatty acid oxidation in the liver is thought to play a significant role in the control of food intake and a low postprandial oxidation of ingested fat may contribute to the overeating on a high-fat diet (Scharrer and Langhans, 1987). The purpose of the present experiment was to evaluate this hypothesis in a strain of rats (Lou/C), characterised by a self-caloric restriction (Couturier et al., 2002). Adult rats (Lou/C and Wistar) were fed either a high-carbohydrate, low-fat diet (HC), or allowed to choose between the HC-diet and a high-fat diet (HF). Fatty oxidation was assessed in vitro in rat liver mitochondria by studying the respiration rates with lipid substrates (octanoyl- and palmitoyl-carnitine) in the presence of increasing concentrations

of acyl-CoA-dehydrogenases inhibitor mercaptoacetate (MA). The orexigenic effects of MA were evaluated in vivo by measuring cumulative food intake during 6 h after MA injection (200, 400 or 600 μmol.kg^{-1}, i.p.). With both octanoyl- and palmitoyl-carnitine, the ADP-stimulated respiration (State 3) was inhibited by MA on the LF diet but (i) the requisite MA dose for inhibition is higher in Lou/C than Wistar rats and (ii) hepatic fatty oxidation in the Lou/c rat remains significantly higher than the Wistar rat irrespective of the MA dose. In vivo, the MA (400 and 600 μmol.kg^{-1}) dose-dependently increased food intake in Wistar rats whereas MA did not trigger any orexigenic effect in Lou/C rats. The HF diet increased β-oxidation in the liver in both rat strains. However, O_2 consumption remains higher in Lou/C rats in the presence of MA. The sensitivity to the orexigenic effects of MA was increased by high fat feeding but the response remained lower in Lou/C at middle and high MA dose. It is likely that the higher capacity of β-oxidation displayed by the Lou/C rat is responsible for the low caloric intake displayed by these rats. The mechanisms by which β-oxidation is perceived by liver cells is currently unknown but could be linked either to energy status (ATP-to-ADP ratio) and/or to the alteration of membrane potential of hepatocytes. In contrary, the lower sensitivity of Lou/C rats to the orexigenic effects of MA could be due to higher acyl-CoA dehydrogenase activity. These hypotheses are currently under investigation.

Effect of a weight-reducing program in obese sedentary pre- and postmenopausal women. S. Lemoine, N. Rossell, V. Drapeau, M. Poulain, F. Sanguignol, P. Mauriège (UFR Staps, Université Paul Sabatier, Toulouse, France).

The aim of this study was to examine the impact of a multidisciplinary weight-reducing program on body composition, physical capacities, health-related quality of life (HRQL), and eating behaviors of obese pre- (38.5 ± 4.5 years, n = 13) and postmenopausal (55.5 ± 4.3 years, n = 27) sedentary women. All subjects received an energy supply close to 1400 ± 200 kcal/day, 6 days per week, during 3 weeks. This program also included 45 min cycle-ergometer endurance and 25 min walking sessions at 50% of heart rate determined at the end of the six-min walking test (6MWT). Body mass index (BMI), fat mass and lean mass assessed by biolectrical impedance, distance walked to 6MWT, HRQL evaluated by the SF-36 questionnaire (physical and mental component scores, PCS and MCS), and eating behaviors (dietary restraint, disinhibition and susceptibility to hunger measured by the Three-Factor Eating Questionnaire) were determined before and after weight loss. BMI and fat mass decreased ($P < 0.0001$) while the distance walked to 6MWT increased in both groups ($P < 0.001$). Although the MCS was higher in both groups ($P < 0.0001$), the PCS only increased in postmenopausal women after weight reduction ($P < 0.001$). The restriction score was increased ($P < 0.0001$), whereas disinhibition and susceptibility to hunger scores were decreased in pre- and postmenopausal women after weight loss ($P < 0.001$ and $P < 0.01$, respectively). Our study shows the efficiency of a multidisciplinary weight-reducing program on anthropometric and physical markers, as well as on HRQL and eating behavior, irrespective of the women's age.

In vivo nutritional control of ChREBP expression: implication in the control of lipogenesis. D. Letexier, O. Peroni, C. Pinteur, B.B. Kahn, M. Beylot (Inserm U499, Faculté RTH Laennec, Rue G. Paradin, 69372 Lyon Cedex 08, France).

The stimulatory effect of glucose on the expression of the lipogenic gene is mediated by ChREBP (carbohydrate response element binding protein) at least in the liver. Glucose is a known stimulator of ChREBP activity but less is known on its expression control; in vitro experiments suggest that its expression is stimulated by insulin and glucose and inhibited by fatty acids. We examined the in vivo nutritional control of ChREBP expression in (i) liver and adipose tissue of Wistar rats (fed and fasted for 48 h) and obese Zucker rats, (ii) adipose tissue of fed mice with specific overexpression (Glut-4 ++) or invalidation (Glut-4 -/-) of Glut-4 in

adipose tissue. Adipose tissue ChREBP mRNA concentrations were increased in Glut-4++and decreased in Glut-4-/- mice suggesting that the uptake and metabolism of glucose adipocyte participate to the control of ChREBP expression. FAS and ACC1 mRNA levels were modified as ChREBP expression whereas SREBP-1c was unchanged suggesting that ChREBP controls FAS and ACC1 expression in adipose tissue. In contrast to these results in genetically modified mice, ChREBP expression was not modified by fasting or high fat diet in both liver and adipose tissue of Wistar rats; the variations of FAS and ACC1 mRNA were positively related to SREBP-1c but not ChREBP expression. Lastly, ChREBP expression was increased in the liver but not in the adipose tissue of obese Zucker rats compared to lean rats. Even if glucose could participate in its regulation, ChREBP expression appears poorly responsive to physiological variations of nutritional conditions. These results support a role of ChREBP in the development of hepatic steatosis and hypertriglyceridemia but not of obesity in the obese Zucker rat model.

Microsomal prostaglandin E2 synthase-1 (mPGES-1) expression is essential for immune-induced anorexia. E. Pecchi, M. Dallaporta, S. Thirion, C. Salvat, F. Berenbaum, A. Jean, J.D. Troadec (UMR 6153 CNRS-1147 Inra, Aix-Marseille III; UMR 7079 CNRS, Paris VI, France).

Infection and inflammation induce a set of non-specific symptoms. Among the behavioural changes observed, anorexia appears advantageous for the host by limiting energy consumption devolved to the research of food and by reducing the nutriments available for microorganisms. However, chronic anorexia compromises immune defences, reduces muscle mass and therefore may represent a significant health risk. Thus, it appears critical to characterise the molecular mechanisms underlying anorexia during infection. Prostaglandins constitute an important inflammatory mediator family whose levels increase in the brain during inflammatory states. The prostaglandin E synthases (PGES) are involved in the production of PGE2 from PGH2. Microsomal PGES-1 (mPGES-1) has been described as an inducible enzyme whose expression is stimulated by pro-inflammatory agents in several tissues. The present study attempted to determine whether an up regulation of mPGES-1 gene expression may account for immune induced anorexic behaviour. In response to anorexic doses of pro-inflammatory cytokines (IL-1β), mPGES-1 gene expression is up-regulated in the two main central structures involved in the control of food intake i.e. the DVC, a brainstem structure lining the 4th ventricle, and the hypothalamus. Interestingly, injection of IL-1β into the 4th ventricle resulted in an mPGES-1 expression increase and a concomitant reduction in food intake suggesting that the DVC plays a preponderant role in the onset of anorexic behaviour. Noteworthy, Il-1β failed to decrease food intake in mPGES-1 KO mice (Pfizer, Groton, USA). Altogether, our results demonstrate that mPGES-1 which is strongly up-regulated in the hypothalamus and the DVC is essential for immune anorexic behaviour and thus constitutes a potential therapeutic target.

Whole-body and lower-limb body composition assessment in senior women. M. Rance, B. Morio, D. Courteix, M. Bedu, E. Van Praagh, P. Duché (Laboratoire Interuniversitaire de Biologie des Activités Physiques et Sportives, UFR Staps Clermont-Ferrand, BP 104, 63172 Aubière Cedex, France).

To evaluate in female seniors, the accuracy and bias of anthropometry and bioelectrical impedance analysis (BIA) for whole-body and lower-limb body composition measures using dual-energy X-ray absorptiometry (DXA) as the criterion method. Nineteen women (66.1 ± 4.2 y) participated in the study. Whole-body fat mass (FM) and fat-free mass (FFM) were measured by anthropometry (A), BIA and DXA. Lower-limb volume (LLV) and FFM (LLFFM) were assessed by anthropometry and DXA. No significant difference was observed between FM^{A} vs. FM^{DEXA} and FFM^{A} vs. FFM^{DEXA} (r^2 = 0.93, $P < 0.001$, CV = 7.3% and r^2 = 0.85, $P <$ 0.001, CV = 4.4%, respectively). No significant difference was observed between FM^{BIA} and

FM^{DEXA} ($r^2 = 0.80$, $P < 0.001$, CV = 11.6%). FFM was significantly underestimated by BIA vs. DXA ($P < 0.01$). LLV and LLFFM were significantly overestimated by anthropometry vs. DXA ($P < 0.05$ and $P < 0.001$, respectively) but significant relationships ($r^2 > 0.25$, $P < 0.001$) were observed. The difference between the right and left lower-limb measures was not affected whatever the method used. In conclusion, in female seniors, (i) anthropometry represents an accurate method to assess whole-body composition which has to be improved by corrective equations before being used to accurately estimate lower-limb body composition; (ii) despite non significant bias for fat mass measurement, bioelectrical impedance analysis tends to overestimate fat mass and underestimate fat-free mass.

Session III. Endocrinology

Evolution kinetics of women waist measurement according to body mass index during endurance training. E. Abid, K Masmoudi, N. Zouari (Functional Exploration Department, CHU H. Bourguiba, 3029 Sfax, Tunisia).

Woman waist measurement (WM) higher than 88cm belongs to elements of metabolic syndrome definition. The aim of our study is to compare the evolution kinetics of WM of obese women, those with weight excess and those with normal weight during 6 months training in endurance: Twenty-nine women (age: 36.8 ± 2.55 y), distributed into 3 groups of respectively 9, 10 and 10 subjects recording to BMI (G1: 22.83 ± 0.42; G2: 26.7 ± 0.42; G3: 33.84 ± 0.83 $kg{\cdot}m^{-2}$) were recruited. An enduring exercise was carried out during 5 meetings per week of 1 h each during 6 m. Measurements of weight, BMI, WM, hip measurement and fatty mass percentage were taken before and then monthly during training. We found a significant decrease of all parameters in Gl and G2. However, in G3, the loss of weight and BMI was not significant in spite of the significant reduction of other measurements. Concerning the WM, its decrease every month was always significant for the 3 groups with a value of $P < 0.001$ during the first months and $P < 0.05$ during the last months. At the end of 6 months, the fall of the absolute value of WM was more marked for G3 but it was comparable between the 3 groups if expressed as a percentage. In conclusion, a maintained physical activity in endurance always has a beneficial effect on the WM. Thus, the perceptible absence of fall of weight among obese women should not discourage them especially since it has a significant reduction of WM which would testify to an improvement of the metabolic syndrome.

Effect of pioglitazone treatment on adipose tissue glucocorticoid (GC) metabolism in adult rats with postnatal diet-induced overweight and metabolic syndrome. S. Boullu-Ciocca, V. Achard, A. Dutour, M. Grino (Laboratory of Hematology, Inserm UMR 626, Faculty of Medicine, University de la Méditerranée, 13916 Marseille, France).

Local reactivation of inert into active GC in visceral adipose tissue (VAT), driven by 11 beta –hydroxysteroid dehydrogenase type 1 (11 beta-HSD-1), plays a pivotal role in the pathophysiology of obesity and the metabolic syndrome. The metabolic actions of pioglitazone are well documented; however, their underlying mechanisms are only partially known. Some experimental studies (in vivo using a genetic model of obesity or in vitro) suggest that 11 beta-HSD-1 can be implicated. We studied the effects of pioglitazone in a model of environmentally (postnatal overfeeding)- induced overweight and metabolic syndrome. Early postnatal (P3-P21) normofed (NF) or overfed (OF) adult rats were treated with pioglitazone for 5 weeks (3 $mg.kg^{-1}.day^{-1}$ per os; Takeda Chemical Industries, Japan). In NF rats, pioglitazone treatment induced a body weight increase but did not affect metabolic and hormonal parameters. OF rats were overweighted, showed glucose intolerance together with increased VAT mass and 11 beta-HSD-1 mRNA expression (44.48 ± 3.08 vs. 35.20 ± 0.64 $nCi.g^{-1}$ in untreated NF; $P < 0.001$). Pioglitazone treatment induced a body weight increase, normalised glucose tolerance, enlarged subcutaneous AT mass, and decreased VAT mass and 11 beta-HSD-1 mRNA expression (37.58 ± 0.64 $nCi.g^{-1}$; $P < 0.05$ vs. untreated

OF rats). These results show that pioglitazone treatment down-regulates adipose tissue 11 beta-HSD-1 expression in a postnatal diet-induced model of overweight and metabolic syndrome. They suggest that drug-induced alterations in local GC metabolism, specifically in VAT, induces, at least in part, fat mass changes and insulin sensitivity improvement.

Altitude-induced anorexia in obese Zucker rats. N. Simler, A. Grosfeld, M. Guerre-Millo, A.X. Bigard (Centre de Recherches du Service de Santé des Armées, 38702 La Tronche, France).

Altitude-induced anorexia is well described in humans and in rodents but the initiating processes remain unknown. A growing number of recent works reported a stimulation of the production of the leptin protein, an adipokine inducing satiety, under low oxygen availability in vitro. We assessed the effects of hypobaric hypoxia (from 1 to 4 days) in lean FA/FA and in obese fa/fa Zucker rats lacking on leptin signaling. Obese and lean rats exhibited a same immediate and marked anorexia. In lean rats, no variation in leptin expression and/or in circulating levels could be seen. Obese rats showed significant increases in both leptin production and release, and in the hypoxia-inducible gene VEGF expression in white adipose tissue. In the hypothalamus, the expression of the orexigenic NPY did not drop at the onset of hypoxia whatever the genotype, and POMC, AGRP, CART and CRF mRNA did not vary. We concluded that altitude-induced anorexia was neither driven by leptin nor by hypothalamic neuropeptides regulating food intake. Nevertheless, the marked stimulation of the leptin gene expression and synthesis in obese rats is in favor of an acute action of ambient hypoxia on leptin gene expression. This specific action of hypoxia in obese rats could be related to the weakness of some counter-regulatory hormonal pathways in the obese phenotype such as the β-adrenergic pathway or to a hypersensitivity of the hypertrophied white adipose tissue toward hypoxia due to reduced local blood flow.

Cell swelling induced peptide hormone secretion. V. Strbak, J. Benický, S.E. Greer, Z. Bacova, M.A. Greer (Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovakia).

Alterations of cell volume represent an independent signal contributing to the regulation of cell function. Cell swelling (induced by hypotonic medium or ethanol in isosmotic medium) evokes the secretion of hormones and peptides stored in secretory vesicles from various types of cells (endocrine, neurons, leukocytes, exocrine pancreas). The dynamics of this secretion is indistinguishable from those induced by specific secretagogues. This type of regulated secretion possesses several specific features. It does not require a rise in intracellular Ca^{2+} through the opening of Ca^{2+} channels. Using various tissues (pituitary, pancreatic islets, heart and brain structures), hormones (prolactin, insulin, thyrotropin releasing hormone – TRH, oxytocin) and inhibitors, we found that hormone secretion induced by cell swelling is not depressed by inhibition of stretch activated channels, mercury-sensitive aquaporins, protein kinase C, microtubules and microfilaments and does not involve prostaglandins and leukotriens. Blocking Na^+-K^+-dependent ATPase, Na^+ channels, K^+ channels or $K^+/Na^+/2Cl^-$ co transport had no inhibiting effect on hyposmolarity-induced hormone secretion in pituitary or pancreatic cells. Careful comparison of glucose and hypotonicity induced secretion revealed a novel signaling pathway for the stimulation of insulin secretion exploited by cell swelling. Hyposmotic stimulation is independent of both extracellular and intracellular Ca^{2+}, does not involve PKC activation, and could not be inhibited by noradrenaline. Participation of such a general phenomenon raises the question of specificity. Cell swelling induced by hypotonicity or isosmotic ethanol containing medium evoked the release of TRH but not oxytocin from the hypothalamic paraventricular nucleus and posterior pituitary. Swelling induced oxytocin release could be uncovered by inhibiting stretch receptors activated channels by GdCl3. In conclusion, cell swelling consistently triggers peptide secretion from various types of cells exploiting a different transduction pathway than that delineated for other natural or pharmacological secretagogues.

Signaling is likely to act at a distal end of the secretory pathway. This stimulation possesses limited selectivity. By overriding physiological inhibition, cell swelling induced secretion might represent important pathophysiological mechanisms.

Session IV. Muscular exercise

Effect of sprint training and detraining on catecholamine responses to sprint exercise in adolescent boys. M. Botcazou, H. Zouhal, C. Jacob, A. Gratas-Delamarche, S. Vincent, D. Bentué-Ferrer, P. Delamarche (Laboratoire de Physiologie, Université Rennes 2, Av. C. Tillon, 35043 Rennes Cedex, France).

Catecholamines (adrenaline (A) + noradrenaline (NA)) are known to play a major role during exercise by controlling hepatic and muscular glycogenolysis (Sonne et al. 1985). Physical training is a potential factor able to alter the sympathoadrenergic activity in response to exercise. Indeed, Strobel et al. (1999) and Zouhal et al. (2001) demonstrated that essentially the intensity of training, such as sprint training, may alter catecholamine responses to exercise. In children, pubertal maturation induces hormonal and metabolic modifications and may influence catecholamine responses to exercise. Thus, we studied the combined effect of sprint training (6 months) and maturation in adolescent boys on plasma A, NA and blood lactate (La) in response to a 6 s-sprint on a cycle ergometer. Thirteen healthy boys (Tanner Stage 4, training group (TG), $n = 6$, control group (CG), $n = 7$) took part in our study and performed a 6s-sprint test before training (P1), after the training period (P2) and after 5 months of detraining (P3) for TG only. Maximal power (Wmax) determined during the 6s-sprint test increased significantly in TG after P2. The performances did not change in CG; Wmax was significantly higher in TG after P2 compared to CG. In response to the 6s-sprint test, La and NA concentrations increased significantly in TG and CG after P1 and P2 and were similar between the groups. However, the 6s-sprint induced significant plasma A increase in TG and CG, only after P2, and in TG after P3. Our data strongly indicate that in adolescent boys, sprint training may enhance performances but not catecholamine response to short cycle ergometer sprinting suggesting an eventual pubertal maturation effect on sympathoadrenergic activity.

VO_2 slow component and fibre recruitment. G. Deley, G.Y. Millet, F. Borrani, G. Lattier, L. Brondel (Inserm/ERITm 0207, UFR Staps, 21000 Dijon, France).

During high-intensity exercises, the oxygen uptake kinetics is characterised by a slow component, which delays or prevents the attainment of the steady state. The aim of this study was to use prior fatiguing exercises to test the hypothesis that recruitment of type II fibers participates in the VO_2 slow component phenomenon. Nine subjects performed three randomised cycling exercises at a work rate corresponding to 80% of their maximal aerobic power: (i) preceded by a fatiguing protocol using electromyostimulation (EMS), (ii) preceded by a fatiguing protocol using voluntary contractions (VOL) and (iii) without the fatiguing protocol (CONTR). The fatiguing protocols consisted in an alternation of 10 s of isometric contractions and 10 s of recovery during 20 min, at 10% of a maximal voluntary contraction (MVC), on the two knee extensors. Respiratory gas exchanges were monitored breath-by-breath during the cycling tests and then analysed with a bi-exponential model. The main result is that a 20-min prior exercise with electrically-induced or voluntary contractions at a same % of MVC induced similar force reduction but affected the VO_2 kinetics differently. The amplitude registered after EMS was significantly reduced and delayed compared with those obtained in CONTR and VOL conditions ($P < 0.05$). Moreover, the cycling test was significantly shorter for EMS than for CONTR and VOL ($P < 0.01$). According to several studies on the recruitment order, it can be considered that a fatiguing protocol using voluntary or electrically evoked contractions affects a different pool of motor units. These results suggest that type II fiber recruitment may be at least in part implicated in the VO_2 slow component phenomenon.

Effect of endurance training on oxydative phosphorylation and H_2O_2 production in isolated rat liver mitochondria. H. Dubouchaud, T. Coisne, R. Favier, X. Leverve (LBFA-Inserm EMI 0221, Université Joseph Fourier, BP 53, 38041 Grenoble Cedex 9, France).

Reactive oxygen species (ROS) are known to be involved in muscle tissue damage induced by exercise. They are also considered as important factors for the control of cellular functions. The mitochondria is one of the major sites of ROS production in cells. Despite the central role of the liver in the whole body metabolism, little is known about the effects of chronic exercise on mitochondrial ROS production in this tissue. The aim of this study was therefore to measure oxygen consumption (JO_2) and H_2O_2 production in isolated liver mitochondria from trained (treadmill running at 25 $m.min^{-1}$, 1 $h.day^{-1}$, 5 $days.week^{-1}$ for 6 weeks) and control rats. Specific substrates and inhibitors of the different complexes of the electron transport chain (ETC) were used to characterise the sites of alterations. The results show that endurance training increased citrate synthase activity in the liver (+17%, $P < 0.05$) as well as cytochrome C oxydase (+50%, $P < 0.05$) and superoxyde dismutase (MnSOD) (+40%, $P < 0.05$) activities in the liver mitochondria. With succinate (substrate of complex II), state 3 (phosphorylating conditions) JO_2 was higher in trained rats (+29%, $P < 0.05$) while H_2O_2 production was lower (–10%, $P < 0.05$). With octanoylcarnitine as a substrate of both complexes I and II, training decreased H_2O_2 production in the basal state (–25%, $P < 0.05$) and in state 3 (–28%, $P < 0.05$). These results suggest that endurance training induces alterations of the ETC in the liver that could contribute to enhance fatty acid utilisation. These alterations could also reduce ROS production in the liver with consequences on cellular functions.

Physical training in adolescent girls with type 1 diabetes mellitus (IDDM). A. Gratas-Delamarche, E. Heyman, C. Toutain, P. Delamarche (Laboratoire de Physiologie et de Biomécanique de l'Exercice Musculaire, ENS Cachan-UFRAPS, Université Rennes 2, Campus La Harpe, Av. Charles Tillon, 35044 Rennes Cedex, France).

Many studies have indicated that the alteration of physical fitness induced by inactivity from childhood to adulthood is exacerbated in patients with IDDM. Especially in girls, puberty is known to be associated with the appearance of growth hormone and insulin resistance, which usually leads to excess weight, glycemic control deterioration and dyslipidemia. Moreover, the beneficial effects of a physical training program have not yet been demonstrated in this specific population. Thus, we investigated for the first time, in IDDM adolescent girls compared to a control group, the effects of a 6 month supervised training program on physical fitness, body composition, glycemic control, insulin resistance factors (leptin, adiponectin, IGF-I) and quality of life. The main results were that this training program succeeded to significantly improve body composition, physical fitness and quality of life and to stop the pubertal leptin increase. Nevertheless, as in other studies concerning either adults or male adolescents, no significant effect was shown on glycemic control. Thus, it appears difficult to improve glycemic control in IDDM adolescents using training per se without insulin and diet counseling. Nevertheless, these findings strongly incite to encourage IDDM adolescent girls to exercise.

Muscle correlates of the increase in VO_{2max} after combined upper limb resistance and lower limb endurance training in healthy elderly. J. Verney, N. Charifi, J. Castells, F. Kadi, C. Denis (Médecine du Sport et Myologie, Unité de recherche PPEH, Hôpital Bellevue, 42055 Saint-Etienne Cedex 2, France).

To investigate whether the improvement in leg and arm VO_{2max} after upper body strength and lower body endurance training respectively are mediated by similar muscle adaptations? Twelve elderly subjects (73 ± 4 years old) trained 3 times a week during 14 weeks. Training consisted in 3 times 12 min of high intensity interval training on bicycle and 3 times 12 min of upper body resistance training. Maximal oxygen uptake was measured with

mechanically braked ergometer for both lower limbs and upper limbs (arm cranking). Muscle cross sectional area (MCSA) was measured using MRI. Muscle biopsies were taken from the vastus lateralis and deltoideus and immunostained with the antibody CD31 for the visualisation of capillaries and the ratio between the length of capillaries in contact with fibre and fibre perimeter (LC/PF index) was measured. Muscle samples were also spectrophotometrically analysed for citrate synthase (CS) activity. VO_{2max} increased significantly by 9% and 16% in legs and arms respectively. MCSA increased significantly in deltoideus (+7%) but not in quadriceps (+2%). The LC/PF index increased significantly in legs (+30%) but not in arms (+14%). CS activity increased significantly in both muscles. In conclusion, the training-induced increase in VO_{2max} is accompanied by capillarisation and metabolic adaptations in legs and by muscle hypertrophy and metabolic adaptations in arms.

Nitrate and nitrite response to a 30s-Wingate test in men and women. S. Vincent, A. Gratas-Delamarche, B. Saiag, J. Callebert, P. Delamarche (Laboratoire de Physiologie, Université Rennes 2, Av. C. Tillon, 35044 Rennes Cedex, France).

NO plays an important role in regulating vascular tone during exercise and during recovery. During submaximal aerobic exercises, changes in the plasma concentration of the end product of NO have been observed in men. To our knowledge, no study has evaluated these changes in response to sprint exercise. However, sprint exercises increase considerably the blood flow, thus sheer stress and catecholamine levels, activators of NO production. So, the aim of this study was to explore nitrate and nitrite (indicator of Nitric oxide production) responses to a very stressful exercise in physically active students of both sexes. Eight men (22.0 ± 0.6 y; 177.7 ± 2.6 cm; 70.1 ± 1.8 kg) and 8 women (19.8 ± 0.7 y; 165.8 ± 1.5 cm; 59.2 ± 1.8 kg) participated in a 30 s Wingate-test on a bicycle ergometer. Plasma lactate (by a microenzymatic method), nitrates+nitrites (by the Griess colorimetric micromethod), 17β-estradiol (17βE2) and progesterone (by RIA) and catecholamine (by HPLC) concentrations were determined at rest, at the end of the warm-up and exercise periods as well as during the recovery (5, 10, 20 and 30 min). The day of the Wingate test, all women were in luteal phase as indicated by their 17β-estradiol and progesterone values (194.4 ± 14.2 pg.mL^{-1} and 13.7 ± 5.0 ng.mL^{-1} respectively). The results showed that plasma lactate, catecholamines and nitrates+nitrites concentrations increase in response to a 30 s Wingate-test but did not differ beween gender. In conclusion, the major finding of this work was that this type of exercise induced NO production represented by an increase in above 25% of [NO_3^- + NO_2^-]. This study failed to show any significant NO production between both sexes, when exercise generates a similar stress level and creates comparable shear stress.

Session V. Neurophysiology

Animal model of obsessive-compulsive disorder in the primate. Role of the thalamo-cortical projections. B. Aouizerate, D. Guehl, V. Amestoy, J. Tignol, B. Bioulac, P. Burbaud (Service de Psychiatrie d'Adultes, Université Victor Segalen Bordeaux 2, Centre Hospitalier Charles Perrens, Centre Carreire, Bordeaux, France).

Obsessive-Compulsive disorder (OCD) is a relatively common and severely disabling psychiatric disease. Although its pathophysiology is still far from resolved, a dysregulation in the fronto-subcortical circuits originating in the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC) is proposed to play a major role in the pathogenesis of OCD. This work was aimed at testing the hypothesis that an enhanced activity in the orbitofrontal and anterior cingulate loops is a central factor in the mediation of OC symptoms. For this purpose, a pharmacological approach was used in Rhesus monkeys, mainly based on intra-thalamic infusions of the $GABA_A$ receptor antagonist bicuculline in order to induce a disinhibition of the thalamo-cortical projections. The subdivisions

of the medial dorsal (MD) and ventral anterior (VA) nuclei of the thalamus, which preferentially project to the OFC and the ACC, were chosen as targets for infusions. Preliminary results showed an exacerbation of behaviors predominantly oriented towards reward (food) delivery when bicuculline was infused into the most medial and posterior region of VA ("pars magnocellularis"), which is the source of vast projections to the OFC and ACC that are both implicated in emotional and motivational components of behavior. In contrast, infusion of bicuculline into the anterior but lateral part of MD ("pars parvocellularis") led to repetitive behavioral shifts (exploration – observation – feeding), with an enhanced sensitivity to certain environmental stimuli. This subdivision of MD is intimately connected to the ACC and the dorso-lateral prefrontal cortex, which is specifically involved in a range of functions including attention, working memory, and planning of action. In conclusion, these findings suggest the importance of the thalamo-cortical projections from discrete regions of MD and VA in the emergence of repetitive behaviors that are reflective of either an exacerbation of emotional and motivational processes, or a putative deterioration of executive functions.

Pain associated to limited dorsiflexion of operated clubfeet in children. C. Beyaert, T. Haumont, J. Paysant, M.A. Haldric, N. Martinet, J.M. André (Laboratoire de Physiologie, Faculté de Médecine, Av. Forêt de Haye, 54511 Vandoeuvre-lès-Nancy, France).

Pain located at the foot instep (P) and limitation of foot to tibia dorsiflexion (DF) are often associated in clubfoot. P was hypothesised to be elicited or increased when maximal DF is forced involving tibio-talar and/or midfoot joints. Seventeen children (12 ± 3 years of age) who reported P on their 21 clubfeet were compared to controls. Maximal DF and P were assessed when sitting, standing on a slope (barefoot and with the foot attached on a small board to allow only tibio-talar joint movement), when walking at a self selected pace and running. P was elicited for 11 clubfeet among all conditions. P was not elicited in sitting (maximal DF 9 ± 9°) but when standing barefoot (intensity 3.1 ± 2.5 (scale 0-10), maximal DF 18 ± 12°) the intensity of which was reduced with the foot attached on a board (1.8 ± 2, $P < 0.05$; maximal DF 20 ± 11°). During running, mean P intensity ($n = 11$) was higher (2.6 ± 1.7, 9 painful clubfeet) than during walking (0.6 ± 1.1, $n = 3$, $P < 0.05$) associated with a higher maximal DF (16 ± 7° versus 11 ± 5°, $P < 0.01$). Maximal DF was higher in controls ($P < 0.05$) than in the painful clubfeet group when standing (44 ± 6°) and running (29 ± 5°). Pain located at the foot instep was elicited or increased when maximal DF was increased but was still lower than the control values, suggesting painful stress located at the tibio-talar and midfoot joints when DF reached its limit. During maximal DF in standing on a slope, reduction in P intensity by immobilizing midfoot joints suggests their contribution in pain.

Study of the modifications of spontaneous baroreflex sensitivity and sympathovagal balance in experienced pilots after an aerobatic flight. C. Dussault, J.C. Jouanin, D. Tran, C.Y. Guezennec (Imassa, Département de Physiologie, BP 73, 91223 Brétigny-sur-Orge Cedex, France).

The aim of this study was to document modifications in spontaneous baroreflex sensitivity (BRS) and disturbances of sympathovagal balance in aerobatic pilots after exposure to "push-pull" accelerations. Five aerobatic pilots performed during a 30-min flight 5 series of 30 s negative spirals (–4 Gz), followed by 30 s of positive spirals (+4 Gz). A stand-test was performed before the flight (T0), immediately after (PF), 1 h after (PF1) and 2 h after (PF2). Inflight HR was recorded on a magnetic tape with a TEAC recorder (HR 30G, TEAC Corporation, Japan). A Finapres apparatus recorded heart rate (HR) and blood pressure during the stand-tests. The inflight HR results show that there was an effect associated with the change from –Gz to +Gz, for all of the spirals ($P = 0.003$). Moreover, this effect on HR response was accentuated during the series ($P = 0.031$). The results show that resting HR was increased at PF ($P < 0.01$). The analysis of spontaneous BRS

did not change at PF compared to T0 but it was higher at PF1 than PF ($P < 0.05$). Sympathetic modulation of HR variability (HRV) tended to increase in the supine position at PF. Parasympathetic modulation of HRV increased at PF2 ($P < 0.001$).This study demonstrates that the spontaneous BRS and HRV are modified during the recovery phase of aerobatic flight including the push-pull manoeuver. The classical increase in sympathetic activity immediately after exercise could be attenuated by the high vagal activity during –Gz accelerations. Spontaneous BRS analysis could be a tool for clinical surveillance of pilots exposed to push-pull accelerations.

Time-frequency analysis of the central effect of angiotensin I and angiotensin II on heart rate variability in trout. F. Lancien, N. Mimassi, D. Mabin, J.C. Le Mével (Laboratoire de Neurophysiologie, U650, Faculté de Médecine, 22 Av. Camille Desmoulins, 29238 Brest, France).

In order to gain new insight into the existence of a brain renin-angiotensin system (RAS) in teleost fish, we investigated in the unanesthetised trout the effects of centrally administered angiotensin (ANG) I and ANG II on heart rate (HR) and heart rate variability (HRV) prior to or after pretreatment of the animals with captopril, an angiotensin-converting enzyme (ACE) inhibitor. Trout were equipped with electrocardiographic electrodes and with an intracerebroventricular (ICV) cannula. The short-time Fourier transform was used to analyse the time course-actions of the angiotensins on HRV. The ICV injection of the vehicle had no effect on the recorded parameters. The ICV injections of ANG I and ANG II at a dose of 5 and 50 pmol induced a marked action on HR and HRV. At a dose of 50 pmol, ANG I and ANG II produced a progressive and significant increase in HR (+36% and +45%, respectively) but elicited a profound decrease in HRV (–88% and –92%, respectively). ICV injection of captopril (10 μg) had no effect on HR or HRV. However, this ACE inhibitor prevented the tachycardia and abolished the decrease in HRV mediated by 50 pmol of ANG I. By contrast, captopril had no effect upon the cardiac actions of 50 pmol of ANG II. These results give the first support for a functional implication of an ACE-like activity in the brain of teleost fish and suggest that the brain RAS in this species of vertebrates may be involved in the control of cardiac chronotropic activity.

The role of the anterior cingulate cortex in learning from past errors. T. Michelet[a], B. Bioulac, D. Guehl, L. Escola, P. Burbaud ([a] Laboratoire de Physiologie et Physiopathologie de la Signalisation Cellulaire, UMR CNRS 5543, Université Victor Segalen Bordeaux 2, 146 rue Léo Saignat, 33076 Bordeaux, France).

Learning from our own mistakes is a key feature of human behaviour, although the mechanisms underlying short-term adaptation to erroneous action are still poorly understood. Since the descriptions of its involvement in the coding of action outcomes, the anterior cingulate cortex (ACC) is thought to play a central role in performance evaluation and especially in error detection. Furthermore, this cortical region occupies a strategic position within a distributed network that integrates environmental information through high-level cognitive and motivational input. To address this problem, we designed a Stroop-like visuo-motor task in monkeys which favours incorrect action. We found that single neurons recorded in the ACC were closely tuned to behavioural performance. First, the activity of most neurons was biased towards the evaluation of erroneous action. Second, the effect of a warning stimulus on neuronal firing was significantly greater after an erroneous response than after a successful one, leading to an improvement in subsequent performance. Third, a significant proportion of ACC neurons exhibited both these evaluative- and strategic-related activity patterns which are the minimal requirement for remedial action. Finally, we found that these monitoring related activities were not directly modulated by cognitive and motivational information but were rather contingent to the subject's engagement in the task. This result brings together different theories of ACC function by demonstrating that effectively, the different components of action monitoring are processed by the same

ACC neurons. Taken together, these data suggest that the ACC serves as a powerful computational locus for rapid corrective adaptation to behavioural error.

An animal model of a spontaneously reversible obstructive sleep apnea syndrome in the monkey. P. Philip, C.E. Gross, J. Taillard, B. Bioulac, C. Guilleminault (Clinique du Sommeil, CHU Pellegrin, place Amélie Raba Léon, 33076 Bordeaux Cedex, France).

The anatomy of the tongue and uvula in monkeys share many similarities with humans, so this species has the closest approximation to the human upper airway than any other species. In this study, we investigated the feasibility of using small monkeys as experimental animals for an obstructive sleep apnea model. Monkeys received intradermal injections of liquid collagen in the uvula, tongue and lateral pharyngeal walls every two weeks. Polysomnography was performed bi-monthly in order to control the impact of injections on breathing events, respiratory effort (as measured by esophageal pressure) and sleep. Before the injections, the three animals showed normal breathing during sleep with a mean of 4.8 ± 2.0 events.h^{-1}. After the injections, a mean of 27.9 ± 19.7 hypopneas.h^{-1} were recorded ($P = 0.023$). Total sleep time was significantly reduced, with a decrease of REM sleep and stage II sleep; however, stage I sleep increased. Collagen injections in the monkey's upper airways can create sleep disordered breathing and abnormal sleep, as seen in apneic patients.

Cortico submental conduction in patients with central neurological swallow dysfunction. E. Verin, J.P. Marie, P. Denis, (Service de Physiologie Digestive, Urinaire, Respiratoire et Sportive, CHU Rouen, 1 rue de Germont, 76031 Rouen Cedex, France).

Submental muscles, including constrictor pharyngeal muscles, are submitted to an automatic control located in the brainstem and to a bilateral cortical control. The aim of our study was to characterise cortical-submental conduction in stroke patients and to correlate it to swallow dysfunction. Fourteen stroke patients with swallow dysfunction (pharyngeal stasis or aspiration) were studied (7 f, 67 ± 10 y). Submental surface electrodes permitted to record the mylohyoideus motor evoked potential (MEP) after focal transcranial magnetic stimulations. Three stimulations of the right and left hemisphere were realised (6 to 8 cm laterally and 2 to 4 cm anteriorly from the vertex), permitting to record left and right MEP and to calculate MEP score (1 normal response; 2: conduction time > 15 ms; 3 no response) for each subject. Swallowing function was evaluated using pharyngeal endoscopy or pharyngeal videomanometry (pharyngeal fluoroscopy coupled with manometry), which permitted to classify the subjects in group 1 (pharyngeal stasis without laryngeal aspiration) and group 2 (laryngeal aspiration or bronchial penetration). In 6 patients, MEP were normal after right and left cortical stimulations, and in 8 subjects, an abnormal submental conduction was recorded (rise in latency or no response), right or left, ipsi or contro lateral. MEP score was significantly higher in group 2 compared to group 1 (6.6 ± 0.7 vs. 4.6 ± 0.3; $P < 0.05$). In conclusion, mylohyoideus MEP in response to focal cortical stimulation should help to define the cortico pharyngeal pathway lesion. Their conduction time alterations were higher in patients with laryngeal aspiration or bronchial penetration, underlining the major role of the oropharynx in the swallowing function.

Session VI. Normal and pathological weight regulation (neurological and endocrinological aspects)

Control of food intake by stimuli originating from the splanchnic area. S. Blat, C.H. Malbert (UMR SENAH, Inra, 35590 Saint-Gilles, France).

In addition to the obvious role of the gut in the digestion and absorption of nutrients, the intestine and associated visceral organs, including the pancreas, liver and visceral adipose depots, have important sensing and signalling roles in the control of food intake. To accomplish this

role, the gut uses neural and endocrine pathways to communicate with controllers of food intake in the hypothalamus and hindbrain. The idea that short-term (e.g., satiety in the immediate postprandial period) and long-term (e.g., satiation maintaining energy homeostasis) food intake are regulated through distinct mechanisms involving the extrinsic nervous system for satiety and hormonal mediators for satiation is no longer popular and evidence has now been raised that nervous and humoral mechanisms act interactively to regulate long-term and short-term food intake. Indeed, mediators that produce a direct stimulation of visceral sensory nerve endings may do so as part of a discrete sensory signalling pathway. In this case, the afferent neuron does not respond directly to a stimulus, but following the release of a mediator from a primary sense cell. Examples of these cells, which effectively act as principal sensory transducers, are enterochromaffin cells, which release 5-hydroxytryptamine and enteroendocrine cells that release cholecystokinin. However, the stimulation of intrinsic nerves can in turn lead to the secretion of hormones controlling satiety and/or satiation. This is the case for the entero-pancreatic nerves studied in our laboratory. Entero-pancreatic nerves directly connect the gut to the pancreas, and their activation by post prandial stimuli participates in insulin secretion, a hormone well known for controlling satiation. Eventually, synergistic nervous and humoral signals originating from the splanchnic area are conveyed to the central nervous system where they are integrated.

The olfactory system as a sensor of nutritional state? A way to regulate food intake. M. Caillol, C. Baly, J. Aïoun, P. Congar, T. Gorojankina, R. Salesse (NOPA-RCC, Inra, 78352 Jouy-en-Josas Cedex, France).

Many animal behaviors are triggered by odorant cues from the environment. In particular, macrosmatic animals rely on olfaction to find and choose their food. Besides, the nutritional status is known to modulate the responses of the main output neurons in the olfactory bulb (OB), the mitral cells, and to modify the pleasantness of food odors. In order to establish a molecular basis for these observations, we looked for the presence of orexigenic and anorectic peptides and their receptors in the first two stages of the olfactory system, the epithelium (OE) and the OB. By immunohistochemistry, RT-PCR and western blot analysis, we demonstrate the presence of orexins and their receptors (OXR), leptin and its receptors (Ob-R) and insulin receptors in both OE and OB. Interestingly, OXR and Ob-Rs are both localised in neurons of the OE, on cilia which express olfactory receptors, and in mitral cells of the OB. In the OE, functional studies demonstrate that OXR activation leads to an intracellular calcium rise, via PLC activation and IP3 synthesis, whereas leptin induces the phosphorylation of the transduction factor Stat3. In the OB, orexins modulate the electrophysiological responses of mitral cells to olfactory nerve stimulation. Furthermore, in the OE, a number of genes display a modified expression of the nutritional status of rats (fed vs. fasted). Altogether, these results show that peptides implied in the regulation of energy homeostasis are present from the first level of the olfactory system, and that the nutritional status could be detected and integrated at a very peripheral level to finely tune the olfactory message to the physiology.

Recent data on adipocyte lipid droplets: relationship with the plasma membrane through caveolar endocytosis of cholesterol. I. Dugail, S. Le Lay, E. Hajduch, X. Le Lièpvre, C. Thiele, P. Ferré, T. Kurzchalia, K. Simons (Inserm U671, Paris, France).

Recent studies on lipid droplets, the specialised organelle for lipid storage, have revealed a complex structure with a phospholipid/cholesterol monolayer around a hydrophobic neutral lipid core. In adipose tissue, these lipid droplets are extremely developed and serve to provide energy from triacylglycerols in case of food deprivation. The adipose tisssue also contains the largest body pool of free-cholesterol, which accumulates from exogenous sources in the lipid droplet. Since fat cells are particularly rich in caveolae, which have been implicated in cholesterol transport, we investigated the dynamics of caveolins in adipocytes and their role in

cholesterol targeting to lipid droplets. We observed that caveolins associated to previously formed lipid droplets in 3T3-L1 adipocytes, only in the late stages of adipocyte differentiation. Moreover, enlarged lipid droplets from obese rat adipocytes were enriched in caveolins. Exogenously added cholesterol induced the rapid translocation of caveolins from the cell surface to lipid droplets. The inhibitory effect of a dominant negative mutant of dynamin (dynK44A), the protein kinase C-dependence of caveolin translocation to lipid droplets, and its modulation by tyrosine kinase inhibitors suggested that a caveolar endocytic process was involved in this targeting. Caveolin-cholesterol complexes on the lipid droplet could be detected by immunoprecipitation or by labelling with a photoactivatable cholesterol analogue. Furthermore, the study of caveolin-1 null mice adipocytes, revealed that caveolin-1 was required to maintain a normal cholesterol content of adipocyte lipid droplets. These observations thus identify a new intracellular route for caveolin between the cell surface of adipoctes and lipid droplets, important for the regulation of the free cholesterol content of this organelle.

Effects of learning by familiarisation on the taste sensitivity to novel foods. A. Faurion, A.M. Pillias, B. Cerf, N. Boireau (NBS-NOPA, Inra, Domaine de Vilvert, Bât. 325, 78352 Jouy-en-Josas, France).

Pure chemicals unknown to subjects were repetitively tested over weeks in order to assess the concentration eliciting the same intensity of perception as a reference that the 30 subjects had been previously familiarised to. Hedonic evaluation, magnitude estimates (M.E.) and food intake were also recorded. The subjects were submitted to fMRI prior to any familiarisation (day 1), after one experimental session and after 12–15 sessions. The results showed a tremendous decrease of the isointense concentrations, together with increased M.E., indicating an increased sensitivity with familiarisation to tastants. fMRI showed plasticity through a modification of the number of activated pixels at the beginning of the familiarisation. Electrophysiological recordings of the chorda tympani taste nerve (CT) in 5 groups of 10 hamsters either drinking water or given the choice of one tastant versus water for 21 days prior to the experiment, showed a significant increase of CT responses to the series of tastants repeated 6 times during the experiment in controls, but no increase to the familiarised tastant in the group that had been previously familiarised to it. Both peripheral and central levels exhibit plasticity of the quantitative taste response with familiarisation.

Subthalamic deep brain stimulation provokes weight gain in Parkinsonian patients. D. Guehl, C. Perlemoine, V. Rigalleau, F. Macia, F. Tison, H. Gin, P. Burbaud (Service d'Explorations Fonctionnelles du Système Nerveux, Hôpital Haut-Lévêque, Av. de Magellan, 33600, Pessac, France).

During the course of Parkinson disease (PD), almost half of the patients experience weight loss which may be as much as 10 kg in approximately a quarter of all cases. This weight loss mainly involves the fat mass rather than the muscular mass and is probably due to increased energy expenditure (EE). The latter may be raised by motor fluctuations and severity of motor symptoms, particularly dyskinesia. Bilateral subthalamic (STN) stimulation has proved effective both on Parkinsonian symptoms and motor fluctuations in severe forms of PD. However, we had noticed that operated patients gain weight during the first year post-op. We demonstrated that STN stimulation in PD induces a significant weight gain (WG) of 9.7 ± 7 kg and BMI increase of + 4.7 $kg.m^{-2}$ twelve months after surgery. These changes appear to be related to a reduction of 16.5% in rest energy expenditure (REE) without daily energy intake (DEI) adjustment. In comparison to a group of non-operated patients, the reduction in lipid (–27%) and protein (–46%) oxydation induced by STN stimulation could also contribute to WG in our series of 19 patients. In addition, we determined the acute effects of STN stimulation and levodopa on REE and substrate oxidation rate. Switching "on" STN stimulation reduced more REE (–17.5%) than levodopa (–8.3%). Lipid oxidation was reduced (–24%) by acute STN

stimulation whereas levodopa reduced glucose oxidation (–37%) with a slight hyperglycaemic effect. Since levodopa decreases glucose oxidation, the post-op reduction of levodopa daily dose could help prevent the effect of weight gain on glycaemia.

Adipose tissue secretory function and body weight regulation. M. Guerre-Millo (U671 Inserm, 15 rue de l'École de Médecine, 75006 Paris, France).

It is now recognised that the white adipose tissue (WAT) produces a variety of bioactive peptides, collectively termed "adipokines". Alteration of WAT mass in obesity markedly affects adipose secretion. Several adipokines are overproduced in the obese state and have been implicated in obesity-associated complications such as hypertension (angiotensinogen), impaired fibrinolysis (PAI-1) and insulin resistance (TNFα, IL-6, resistin). Conversely, leptin and adiponectin both exert an insulin-sensitizing effect, at least in part by favoring tissue fatty-acid oxidation through activation of AMP-activated kinase (AMPK). Besides, leptin and adiponectin have distinct properties. On the one hand, leptin, which is produced in relation to adipose tissue mass, targets the hypothalamus and allows adapting the rate of food intake to the level of energy store. Mutations in the leptin or leptin receptor gene result in hyperphagia and obesity. These abnormalities are reversed by leptin treatment in leptin-deficient individuals. However, leptin treatment is inefficient in common obesity, which is characterised by hyperleptinemia and resistance to leptin. On the other hand, adiponectin exerts a potent anti-atherogenic effect in cellular and rodent models of atherosclerosis. In humans, low adiponectinemia is associated with increased risk of cardiovascular diseases. A recent study revealed that intracerebroventricular administration of adiponectin in mice resulted in weight loss. On the contrary to leptin, this effect did not rely on reduced food intake but rather on increased oxygen consumption (VO_2) and thermogenesis. Thus, through its secretory function, WAT lies at the heart of a complex network of factors capable of influencing several physiological processes, energy homeostasis and body weight regulation. Some adipokines, like leptin and adiponectin, exert a beneficial effect on energy balance, insulin action and vasculature, while the excessive production of other adipokines could be deleterious in obesity.

Brainstem neuroplasticity and control of food intake. A. Jean, B. Bariohay, C. Charrier, M. Dallaporta, E. Pecchi, B. Felix, B. Lebrun, J.D. Troadec, E. Moyse (Physiologie Neurovégétative, UMR CNRS-Inra-Université Paul Cézanne, Faculté des Sciences et Techniques, 13397 Marseille Cedex 20, France).

Classically, the neural control of food intake depends on (i) hypothalamic nuclei which integrate adiposity signals, secreted proportionally to the fat stores, and (ii) the dorsal vagal complex (DVC) of the brainstem which integrates satiety signals produced in the oro-gastro-intestinal tract during eating to determine meal size. Recent results indicate that the neuroplasticity phenomena within the hypothalamus play a role in the mechanisms regulating food intake. The DVC of the adult has also been recently shown to be a site of important neuroplasticity: (i) the DVC displays high content of PSA-NCAM, GAP-43 and BDNF; (ii) it is a site of neurogenesis; (iii) its glial environment could be a support of the observed neurogenesis. We addressed the question whether brainstem elements involved in neuroplasticity are also involved in the control of food intake. The results already obtained show that BDNF plays a role as an anorexigenic factor within the DVC: (i) BDNF infusions in the DVC induced anorexia, weight loss and inhibited swallowing, a fundamental motor component of food intake behaviour; (ii) BDNF protein content was down-regulated by fasting and transiently up-regulated by leptin or CCK peripheral treatment. Preliminary results show that the DVC glial compartment could also be involved in the regulation of food intake: (iii) modification of astrocyte metabolism by methionine sulfoximide (MSO) decreased food intake and body weight; (iv) MSO treatment suppressed the alimentary response to 2-deoxyglucose as well as c-fos activation within the DVC. These results

indicate that the DVC plays a crucial role in the control of food intake and that the mechanisms involved are far to be underlained only by hard-wired reflex circuits.

Session VII. Respiration

Differential kinetics of airway response to histamine aerosol in central and peripheral airways studied by synchrotron radiation ct imaging in the rabbit. S. Bayat, L. Porra, H. Suhonen, N. Christian, P. Suortti, A.R.A. Sovijärvi (European Synchrotron Radiation Facility, Grenoble, France).

Although airway hyper-reactivity is the hallmark of bronchial asthma, regional kinetics of airway narrowing are not well understood. We applied a novel CT imaging technique using synchrotron radiation to image stable xenon gas within the airways and peripheral air spaces (Porra et al., J Appl Physiol 2004, 96: 1899; Monfraix et al., Phys Med Biol 2005, 50: 1) in order to study the kinetics of central and peripheral airway response to histamine aerosol in healthy anesthetised and mechanically ventilated rabbits up to 60 min after histamine administration. Individual proximal airway constriction was assessed by measuring the luminal Cross-Sectional Area (CSA). Peripheral airway obstruction was estimated by measuring the Ventilated Alveolar Area (VAA) following inhaled Xe administration. Overall thoracopulmonary resistance (RLT) was assessed continuously. Proximal airway CSA decreased by 60% of the baseline value in 20 min and recovered gradually by 60 min. The VAA decreased immediately after histamine inhalation by 50% of the baseline value and recovered rapidly thereafter. The results indicate significantly slower airway response and recovery in central vs. peripheral airways in the rabbit. The kinetics of RLT appeared to be the sum of central and peripheral airway contributions. In conclusion, we found significant differences in the kinetics of histamine response in central vs. peripheral airways, as well as differences in airway reactivity as a function of airway size in central airways.

Influence of a rehabilitation training program of "swimming" on ventilatory function in a young tetraplegic. B. Beaune, J. Perrot, D. Colin (Laboratoire des APS, Université du Maine, Av. Olivier Messiaen, 72085 Le Mans Cedex 9, France).

The aim of our study was to evaluate the consequences of a rehabilitation training program of "swimming" for 5 weeks (1–2 sessions per week, 45 min per session) on ventilatory function (tidal (TV), inspiratory reserve (IRV), expiratory reserve (ERV) volumes, vital capacity (VC), forced expiratory volume in 1 s (FEV1), maximal expiratory-flow volume (MEFV), time of apnea (TA)) in a male patient, C5-C6 tetraplegic for two years, 17 year-old and without any lung physiotherapy program. Before training, the patient exhibits a strong ventilatory deficiency, comparable to "pulmonary restrictive syndrome" with normal TV values only (0.7 L). At the end of the training program, all volumes and capacities were enhanced (IRV: +51%; ERV: +195%; VC: +48%) except TV (–14%). FEV1 and MEFV increased by 81% and 161%, respectively, and TA rose from 32 to 52 seconds (+63%). All these results show that a well-adaptated training program of "swimming" in tetraplegic patient permits successful but partial lung rehabilitation and allows for benefits compatible with increased autonomy.

Structure-function relationship in human bronchial obstruction. P. Berger (Laboratoire de Physiologie Cellulaire Respiratoire, Inserm E356, Université Bordeaux 2, Service d'Exploration Fonctionnelle Respiratoire, Hôpital Haut-Lévêque, CHU Bordeaux, France).

Airway wall remodeling observed in chronic obstructive pulmonary disease (COPD) contributes to alteration in the function of the airways. Air trapping within the peripheral airways can be evaluated by lung attenuation measurement using quantitative computed tomography (CT). Airway thickening within the proximal airways can also be evaluated using CT and a dedicated software tool based on a

Laplacian of Gaussian algorithm. Such CT data can thus be compared to both in vitro assessment of airway smooth muscle responsiveness and inflammatory cell infiltration and in vivo lung function testing measurements. Different groups of patients have been included i.e., ex- or current smokers with or without functional obstruction, and healthy non smoking subjects. In a first study, we demonstrated that, in smokers, air trapping assessed by the difference between inspiratory and expiratory attenuation was correlated with an inflammatory infiltration of the smooth muscle layer of small airways. This cell infiltration involved mainly mast cells and increased with the decrease of in vitro relaxation to salbutamol. In a second study, we validated software for 2D images allowing the assessment of different proximal bronchial parameters including wall area (WA), internal area (IA). The ratio of the sum of WA to the sum of IA (i.e, ΣWA/ΣIA) which reflected normalised airway thickening, was significantly different between patients diagnosed with COPD, smokers and control subjects. Normalised airway thickening and internal area were significantly related to lung function testing data, including FEV1, sGaw, FEF25-75. Finally, we developed new 3D software that enabled us to localise airway remodeling in COPD between the sixth and the eighth bronchial generation. These works were funded by PHRC 1997 and 2002.

Assessment of the ventilatory thresholds from heart rate variability in adolescent triathletes and adult cyclists. F. Cottin, P.M. Leprêtre, P. Lopes, Y. Papelier, C. Médigue, V. Billat (Laboratory of Exercise Physiology (LEPH), University of Evry, EA 3872, Genopôle, Bd F. Mitterrand, 91025 Evry Cedex, France).

The purpose of this study was to examine whether it is possible to assess ventilatory thresholds from heart rate variability (HRV) analysis in healthy well-trained subjects. ECG, VO_2, VCO_2, V_E and blood lactate concentration of sixteen well-trained adult cyclists (C, $n = 8$) and young triathletes (T, $n = 8$) were collected during an incremental exhaustive test performed on a cycloergometer. The "Short-Term Fourier Transform" analysis was applied to RR time series to compute usual HRV components vs. power stages. For all subjects, visual examination of both ventilatory equivalents and instantaneous high-frequency (HF) energy multiplied by the instantaneous frequency of the HF peak (HF.f_{HF}, HF: 0.15-*fmax* Hz) vs. time (linked to power stages) has shown two synchronous abrupt increases, at the same power level, giving the first ventilatory threshold (VT1) associated with the first HF threshold (HFT1), and the second ventilatory threshold (VT2) associated with the second HF threshold (HFT2). When expressed as a function of power, HFT1 and HFT2 were not respectively different from VT1 and VT2 in C and T. In addition, HFT1 and HFT2 were respectively strongly correlated to VT1 (C: $r^2 = 0.97$, T: $r^2 = 0.96$, $P < 0.001$) and VT2 (C: $r^2 = 0.94$, T: $r^2 = 0.97$, $P < 0.001$). The subject characteristics and physiological performance levels of the two groups in absolute terms were all significantly different. However, when the performance values were normalised, no significant difference was found between cyclists and triathletes. This study shows that ventilatory threshold assessment is possible from cardiac RR time series using HRV time-frequency analysis in healthy well-trained athletes.

Does the meconial aspiration syndrome affect long term pulmonary function? N. Djemal, K. Masmoudi, H. Ben Amar, N. Zouari (Functional Exploration Department, Bourguiba University Hospital, 3029 Sfax, Tunisia).

Acute pulmonary consequences of the meconium aspiration syndrome (MAS) are well described. However, few studies of the long term pulmonary sequelae in MAS have been made. In order to evaluate long term pulmonary function in MAS survivors, we studied 14 children aged 4 to 11 years, an average of 7.41 ± 2.27 years after injury. Our sample had a mean weight of 24.6 ± 7.35 kg and a mean height of 124.5 cm ± 10.64. At birth, the mean Apgar scores respectively at 1 and 5 min were 5.3 ± 2.28 and 7.23 ± 1.74. All 14 children required oxygen for a mean period of 6.35 days ± 4.95. In the current study, the

parents answered a questionnaire to evaluate clinical pulmonary and cognitive functions of their children. In each child, complete spirometry was fulfilled. An exercise stress test on an ergocycle was achieved only by seven children. Respiratory symptoms such as wheezing episodes and respiratory tract infections were found respectively in an average frequency of 2 ± 1.73 episodes/year and 4.35 ± 3.36 episodes/year. Two children had exercise intolerance. Spirometry displayed FEV1, Tiffeneau ratio (FEV1/FVC), TLC and FRC respectively in an average of 90.35 ± 1 7.75% th, 90.92 ± 5.81% th, 171 ± 64.76% th and 286.5 ± 135.96%. The exercise stress test revealed a mean VO_{2max} of 90.3% ± 14.56. Spirometry realised 5, 10 and 15 min after exercise showed an FEV1 reduction of respectively 8.5, 12.25 and 11%. We conclude that children surviving MAS have long term pulmonary sequelae, including alveolar hyperinflation and airway hyper reactivity to exercise.

Antioxidative efficacy of resveratrol against hepatic damage induced by chronic ethanol administration in rats. A. Kasdallah-Grissa, B. Mornagui, H. Ben Gharbia, A. Nahdi, N. Gharbi, M. Hammami, S. El-Fazaâ (Laboratoire de Physiologie Animale, Département de Biologie, Faculté des Sciences de Tunis, Campus Universitaire 1060, Tunis, Tunisia).

The chronic consumption of alcoholic beverages is a major cause of liver injury and the development of serious liver disease. Hepatotoxicity of ethanol is well recognised to be associated with the formation of free radicals, lipid peroxidation and oxidative stress. Therefore, the potential role of several antioxidant substances such as vitamins and polyphenols has been investigated in ethanol-induced liver injury. Resveratrol (trans-3,4',5-trihydroxystilbene) is a naturally occurring phytoalexin present in grapes and other plants which have long been used in traditional oriental medicine. It was recently found that this compound possesses a variety of biological activities and exhibits antioxidant properties. This prompted us to investigate whether this polyphenolic compound is capable of exerting any protective effects in face of chronic ethanol-induced liver damage. Three groups of male Wistar rats were used. The first group served as controls and received a daily intraperitoneal (i.p.) injection of 0.9% saline. The second group of rats was treated daily with an i.p. dose of 35% ethanol at 3 $g.kg^{-1}$ body weight. The third group of rats was given the same dose of ethanol but allowed a basal diet supplemented with 5 $g.kg^{-1}$ resveratrol. Chronic ethanol administration for 6 weeks produced hepatotoxicity. This was clearly evident by the increase ($P < 0.05$) in the level of hepatic marker enzymes such as serum transaminases, alkaline phosphatase and gamma glutamyl transferase levels. Alcohol administration improved ($P < 0.01$) the formation of malondialdehyde in the liver indicating an enhancement of lipid peroxidation, the major end-point of oxidative damage. Drastic alterations were observed in the antioxidant defense system, which were reflected by decreased ($P < 0.01$) activities of hepatic superoxide dismutase and glutathione peroxidase. The addition of resveratrol to the diet of alcohol treated rats ameliorated the liver function, inhibited the hepatic peroxidation of lipids, and improved the antioxidant defense system. The levels of all these parameters in alcohol treated rats given a resveratrol supplemented diet were not different from those of controls. These results demonstrate a potent suppressive effect of resveratrol on hepatic toxicity and oxidative damage induced by chronic ethanol administration, suggesting a therapeutic potential for this compound in liver diseases.

Bronchodilation induced by deep inhalation correlates with a decrease in FEV1/FVC during exercise induced airway obstruction in children. F. Marchal, C. Schweitzer, Y. Thi Nguyen, Lan Vu Thi Thuy, C. Chone, B. Demoulin (Service d'Explorations Fonctionnelles Pédiatriques, Hôpital d'Enfants, allée du Morvan, 54500Vandoeuvre-lés-Nancy, France).

During airway challenge, it has been hypothesised that an isolated decrease in FEV1 expresses constriction of larger airways while an associated decrease in FVC relates to closure of smaller airways. A decrease in FEV1/FVC

should therefore indicate central airway contraction. A deep inhalation (DI) may relieve smooth muscle constriction in these airways because they are subjected to parenchymal tethering. This effect should be reflected in a change in respiratory conductance at 12 Hz (Grs), which more specifically assesses central airway mechanics. Sixty-two children (7–16 years) with suspected asthma and normal baseline lung function were studied before and 5 min after a free run. FEV1 and FVC were obtained by spirometry and Grs by the forced oscillation technique. The Grs response to DI (Grs_{DI}) was calculated as the post- to pre-DI Grs ratio. After exercise, there was a significant decrease in FEV1, FVC and FEV1/FVC and a significant increase in Grs_{DI}. A highly significant correlation was disclosed between the decrease in FEV1/FVC – but not in FVC – and the increase in Grs_{DI} ($P < 0.0001$). The data are consistent with central airway constriction being a significant component of exercise induced airway obstruction, reflected by a decrease in FEV1/FVC and relieved by DI.

Physiological effects of 6-month home training, after 10 weeks of institutionalised respiratory rehabilitation, in COPD patients. J.M. Perruchini, V. Van Wymelbeke, J. Barthe, M. Merati, C. Vassard, L. Jeannin, L. Brondel (A.D.R.RES, 10 rue de Genève, 21000 Dijon, France).

In Chronic Obstructive Pulmonary Disease (COPD) patients, pulmonary Rehabilitation in Institution (R_i) during a limited period improves exercise capacity and decreases respiratory distress. When patients come back home, benefits of R_i are generally lost if home training (T_h) is not pursued. The aim of this study was to evaluate the physiological effects in COPD patients of 10 weeks of R_i, followed by 6 months of T_h. Thirty patients (65 ± 10 years), followed R_i with 3 sessions.week^{-1} (50 min cycling, 30 min respiratory physiotherapy, 45 min quadriceps exercise, 45 min global gymnastics and swimming or relaxation). T_h was composed of 3 sessions/week (50 min cycling and 10 min respiratory physiotherapy) under physiotherapy and technical assistance. The evaluations consisted of lung function and exercise testing, measurements of walking performance and evaluation of the quality of life. There were no changes in lung function parameters during the whole rehabilitation program. In contrast, some parameters related with physical condition or quality of life increased during R_i, but also during T_h, as shown through VO_{2max}, power max, anaerobic threshold, VE/VCO_2, oxygen pulse (VO_2/Fc) and total score of quality of life ($P < 0.05$). During R_i, improvement of life-quality was correlated with a rise in VO_{2max} ($r = 0.426$, $P < 0.05$) and VE/VCO_2 ($r = 0.712$, $P < 0.05$) and during T_h it was correlated with a rise in VO_2/Fc ($r = 0.403$, $P < 0.05$). In conclusion, COPD patients who completed a 6-month program of T_h after 10 weeks of R_i do continue to improve their exercise tolerance and their life-quality by an amelioration of cardiovascular function and/or a better muscular extraction of oxygen.

The effect of puberty on lung function in Tunisian children. Y. Trabelsi, A. Bouchez Buvry, Z. Tabka, N. Gharbi, A. Bienvenue, J.P. Richalet, H. Guenard, A. Zbidi (Department of Physiology and lung function testing, Sousse Faculty of Medicine, University of Sousse, Av. Mohamed Karoui, 4002 Sousse, Tunisia).

Puberty is one of the most important steps in life, involving dramatic morphological and physiological changes. In Tunisian children, nothing is known about the growth of ventilatory function and pubertal stage. The aim of the study was to adjust the relationship between anthropometric parameters and pubertal stage and to produce reference values for spirometric lung function according to the pubertal status in Tunisian children. Pulmonary function values were performed with a Minato portable spirometer in 684 healthy Tunisian children (351 males and 333 females) 8–16 years of age. Pubertal status was assessed for males and females according to the Tanner method. In males and females, height and age were well correlated with pubertal stage. Forced vital capacity and flow expiratory volume in 1 second increased with pubertal stage. Puberty began and ended earlier in females than in boys.

In conclusion, ventilatory function of healthy Tunisian school children increases proportionally with age, height and pubertal stage. This study confirmed that lung growth is of short duration and occurs earlier in females than in males in the pubertal process. These data are of importance to follow the children suffering from chronic pulmonary diseases during puberty.

Session VII. Oxydative stress

Oxidative stress and anaerobic exercise. C. Groussard (Laboratoire de Physiologie et de Biomécanique de l'Exercice Musculaire, UFRAPS Rennes 2, EA 1274, Av. Charles Tillon, Campus la Harpe, CS 24414, 35044 Rennes Cedex, France).

Literature data concerning aerobic exercises and oxidative damages are consistent and have been well documented over the last 25 years. It is now well known that the major factor responsible for oxidative damage during aerobic exercise is the increase in oxygen consumption. However, many other factors known to induce oxidative stress, such as xanthine oxidase activation (Mc Cord, 1985), acidosis (Siesjo et al., 1985) and catecholamine autoxidation (Cohen and Heikkila, 1974) might be operative to a greater extent during anaerobic exercise. All these factors lead then to the hypothesis that even a non aerobic exercise could also induce oxidative stress. However, little attention has been directed towards identifying (i) the changes in oxidative stress markers and antioxidants in response to anaerobic exercise and (ii) the possible sources of reactive oxygen and nitrogen species (RONS) production during this type of exercise. The aim of this symposium is to briefly review the recent publications dealing with oxidative stress and anaerobic exercise and the possible sources of RONS production during this type of exercise.

Influence of self low caloric intake and spontaneous running wheel activity on mitochondrial free radical production. R. Favier, B. Garait, G. Lacraz, K. Couturier (Fundamental and Applied Bioenergetics, EMI 221, Joseph Fourier University, 2280 rue de la Piscine, BP 53X -38041, Grenoble Cedex 9, France).

It has previously been shown that both caloric restriction and chronic exercise are able to modulate mitochondrial free radical generation offering a plausible mechanism by which these interventions could slow down the rate of aging. In the present study, we evaluated the rate of hydrogen peroxide (H_2O_2) production by skeletal muscle mitochondria isolated from a peculiar strain of rats named Lou/C. These rats are characterised by low energy intake (Couturier et al., Int J Obes Relat Metab Disord, 2004) and high voluntary running wheel activity (Servais et al., Free Rad Biol Med, 2003). A group of Lou/C rats was chronically exercised with running wheels (CEL/C) and compared to sedentary Lou/C rats (SedL/C). In addition, SedL/C were compared to sedentary Wistar (SedW) rats. Mitochondria were isolated from the quadriceps, and incubated with substrates providing reducing equivalents to complex I and/or complex II of the mitochondrial electron transport chain (ETC). Mitochondrial H_2O_2 production was significantly reduced in SedL/C as compared to SedW, a decrease that is not linked to reduced oxygen flow through the mitochondria, but rather to an increased expression of uncoupling proteins (UCP-2, UCP-3) and a reduced activity of complex I of the ETC. However, chronic exercise for months did not enhance H_2O_2 production by skeletal muscle mitochondria. In conclusion, the results of this study show that low eater and high runner Lou/C rats are particularly suitable for further study of the mechanisms implicated in the modulation of mitochondrial free radical generation.

Oral communications

Exercise-induced hypoxemia disappeared during 24 h cycling in highly trained subjects. L. Brondel, D. Callard, J.C. Guilland, D. Moreau, J. Van Hoecke, D. Davenne (Centre des Sciences du Goût, 15 rue Hugues Picardet, 21000 Dijon, France).

Heavy short-term aerobic exercise induces hypoxemia (EIH) in certain endurance-trained elite athletes. Nothing is known about hypoxemia evolution during long-term aerobic exercise. In order to evaluate this evolution, 9 male endurance-trained master athletes (age: 38 ± 6 years; VO_{2max} 46.5 ± 4.6 $mL.min^{-1}.kg^{-1}$) and 6 control male subjects (35 ± 8 years; 39.0 ± 9.3 $mL.min^{-1}.kg^{-1}$) participated in the study. The 24h-exercise was conducted using cyclosimulator bicycle trainers. Constant exercise power (60.3 ± 4.1% of maximal aerobic speed) was imposed but interrupted every 4 h by 20 min rest periods. Capillary blood gases were determined before and 1.5, 5.5, 17.5 and 21.5 h after the beginning of cycling. Pulmonary ventilation, VO_2 and non-invasive cardiac output (NICO) were evaluated every 4 h during 10 min. The results show that the "distance covered" was 551.2 ± 36.5 km. EIH was observed 1.5 h after the beginning of exercise ($P < 0.01$) but disappeared later on ($P < 0.05$): PaO_2 values were 92.0 ± 7.8 mmHg at rest and 81.3 ± 8.2, 85.6 ± 5.0, 91.6 ± 4.1 and 84.8 ± 5.9 mmHg during exercise. No change in PaO_2 was observed in control subjects. PaO_2 was correlated with $PaCO_2$ ($r = -871$, $P < 0.01$) and pH ($r = -0.838$, $P < 0.01$). The disappearance of EIH between 1.5 h and 17.5 h was not associated with significant variations in VE, FR, VA, VO_2, VCO_2, VO_2/Fc, NICO, subjects' temperature but with decreases in $P(A\text{-}a)O_2$, pulmonary shunt, V_D, V_D/V_T (respectively, $r = -0.889$, $r = -0.988$, $r = -0.902$, $r = -0.949$, $P < 0.01$) and increases in VE/VO_2, VE/VCO_2, ($r = 0.928$ and $r = 0.935$, $P < 0.01$). So it appears that EIH is a transient situation which could be due to a VA/Q mismatch.

Prognostic value of hematocrit in patients with severe chronic obstructive pulmonary disease receiving long term oxygen therapy. A. Chambellan, E. Chailleux, T. Similowski, the ANTADIR Observatory Group (Institut du Thorax, CHU Nantes, 44093 Nantes Cedex 1, France).

Although traditionally associated with polycythemia, chronic obstructive pulmonary disease (COPD) has a systemic inflammatory component that could interfere with erythropoiesis. This study was aimed at describing the distribution and prognostic value of hematocrit (Ht) in severe COPD patients prescribed long-term oxygen therapy (LTOT). Two thousand five hundred and twenty-four patients with COPD, $FEV_1/VC < 70\%$, $FEV_1 < 80\%$ pred, and $PaO_2 < 7.3$ kPa in whom hematocrit (Ht) was available at entry were identified between 1980 and 1999 in the French ANTADIR chronic respiratory insufficiency and home care database (M/F 5:1, men 68 ± 10 years, women 70 ± 10). Correlation between Ht, demographic data and pulmonary function data were examined. A multivariate Cox proportional hazard regression was performed to identify prognostic factors. Mean Ht was 45.9 ± 7.0% in men and 43.9 ± 6.0% in women. Ht was below 39% in 12.6% of men and below 36% in 8.2% of women (WHO definition of anemia). Ht was negatively correlated with age ($r = -0.245$) and FEV1/VC ($r = -0.068$). It was positively correlated with $PaCO_2$ ($r = 0.161$) and body mass index (BMI) ($r = 0.127$). Multivariate analysis found Ht as an independent predictor of survival, hospital admission rate, and cumulative duration of hospitalisation. The 3-years survival was 24% (95%CI 16–33%) when Ht < 35% and 70% (63–76%) when Ht ≥ 55%. In conclusion, low Ht is not uncommon in LTOT-COPD patients. Ht is negatively associated with mortality and morbidity. Whether the association is causative or not and whether or not corrective measures are warranted remain to be determined.

Kinetic distribution of LiveR and muscle glycogen during exercise induced glycogenolysis. A. Chaouachi, A. Melançon, D. Massicotte, F. Péronnet, C. Lavoie (Centre National de la Médecine et des Sciences du Sport, Tunis, Tunisia).

The objective of the study was to document the effect of three exercise durations on liver and muscular glycogen distribution within desmosglycosomes (acid resistant glycosomes) and lyoglycosomes (acid labile glycosomes). Sprague Dawley rats were randomly submitted to one of the following groups: rest and swimming exercise: 45, 90 or 180 min. The

animals were sacrificed and the rectus femoris and the liver were obtained to measure total glycogen content as well as glycogen associated with desmo- and lyoglycosomes. In both the liver and muscle, exercise depleted ($P < 0.05$) total glycogen content and glycogen associated within both glycosomes. The depletion increased with the duration of exercise. Glycogen distribution between desmo- and lyoglycosomes was 40%: 60% in the liver and 75%: 25% in the muscle in the resting group. These percentages were modified with exercise durations in both tissues. In the liver, changes in glycogen distribution were observed after 90 and 180 min of exercise reaching 60% ($P < 0.05$) and 75% ($P < 0.05$) in desmoglycosomes, respectively. In the muscle, changes in glycogen distribution were rapidly observed reaching 78% after 45 min, 71% after 90 min and 100% after 180 min ($P < 0.05$) in desmoglycosomes. During exercise, glycogenolysis was higher in lyoglycosomes than in desmoglycosomes in the liver ($P < 0.05$). In contrast, in the muscle, glycogenolysis was higher in desmoglycomes ($P < 0.05$). In conclusion, these results suggest that exercise modifies the intracellular distribution of glycogen within desmo- and lyoglycosomes, and that the contribution to energy supply of the two glycogen subfractions is heteregenous and different between the muscle and liver, during exercise.

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Effect of fastskin suits on performance drag and energy cost of swimming. J.C. Chatard, B.D. Wilson (Service de Physiologie Clinique et de l'Exercice, CHU St-Étienne, 42 055 St-Étienne Cedex 2, France).

Fastskin Full Body Suits (FB) have been claimed by manufacturers to reduce passive drag by as much as 10% compared to normal suits (N). However, the manufacturer's claims have not been backed by published peer reviewed studies. This study was undertaken to determine the effect of fastskin suits on swimming performance, drag and energy cost of swimming. Fourteen competitive swimmers swam at maximal effort in a 25 m pool for distances of 25 m, 50 m, 100 m, 200 m, 400 m and 800 m when wearing FB, legs only (L) and N. They performed 4 min swims at their 800 m pace when wearing FB, L, and N, in the swimming flume of the University of Otago, Dunedin NZ. Oxygen consumption was determined using a metabolic cart. Passive drag measures were made when wearing FB, L, and N at speeds between 1.20 and 2.00 $m.s^{-1}$. The order of all suit and performance conditions were randomly assigned. The FB and L suits were purchased from local suppliers and supplied to swimmers according to their fit. There was a 3.42 ± 0.86% performance benefit (decreased swim time) for all swimming distances when wearing the FB. The gain was significantly lower when wearing L (1.93 ± 0.69%, $P < 0.01$). There was a significant reduction in drag (6.15 ± 7.93% vs. 4.73 ± 4.74) and oxygen cost (5.51 ± 3.01% vs. 4.04 ± 5.54%) when wearing FB and L compared to N. However, the difference between FB and L were not significant. In conclusion, there appears to be a performance benefit, and drag and oxygen consumption reduction when wearing FB and L compared to N.

Effect of instruction on the reliability of maximal voluntary force and maximal rate of force development during isometric contraction. T. Driss, R. Sahaly, H. Vandewalle, L. Isère, A. Le Pellec-Muller, H. Monod (GPBM, E.A. 2931, UFR STAPS, Université Paris X, 200 Av. de la république, 92000 Nanterre, France).

Several studies have shown the importance of the instruction on maximal voluntary force (MVF) and maximal rate of force development (MRFD) (Bemben et al., 1990; Christ et al., 1993; Sahaly et al., 2001, 2003). MRFD is slower when the subjects are instructed to produce their "maximal peak force as fast as possible" than when they are instructed "to focus on MRFD" (Sahaly et al., 2001). The reliability of isometric strength indices is high (Viitasalo et al., 1980; Bemben et al., 1990; Sleivert et al., 1994; Mirkov et al., 2004). However, the effect of instruction on the reliability of explosive force indices has not been studied.

We compared the reliability of MRFD and MVF measured with Hard-and-Fast instruction (INST 1) vs. Fast instruction (INST2) in 11 men and 12 women. MVF and MRFD were measured in 3 sessions at one week intervals at the same hour with both protocols. The force-time curve was recorded during unilateral maximal isometric knee extensions. After familiarisation, the subjects performed three trials for both protocols and legs. Reliability was studied by means of ICC and SEE%. ICC of MRFD ranged from 0.42 to 0.92 for INST 1 and from 0.71 to 0.94 for INST 2. ICC of MVF were similar for instructions 1 and 2 and ranged from 0.91 to 0.99. SEE% of MRFD was higher compared to MVF. SEE% of MRFD was lower with INST 2 in both legs and genders. In agreement with Viitasalo et al. and Sleivert et al., the results of the present study suggest that reliability is better for MVF compared to MRFD.

An original method to measure aerobic and anaerobic energy expenditure of in the field physical activities with one high-fixed camera. J.P. Eclache, F. Botton (Laboratoire de la Performance ASTB, 10 rue des Tulipes, 69680 Chassieu, France).

In the field energy expenditure (EE) determinations often increase actual EE and/or solely measure aerobic metabolism. This cheap method requires four stages. First: the determination of the main fundamental activities FA characterised by specific muscular groups and movements. For each FAl of some seconds duration or more, the mechanical variable with the major statistical weight on EE and an event for end-time are selected, generally speed S and u-turn time; for short event FA such as jumping, shooting, striking, throwing, start, event frequency F. Secondly, the experimental subjects achieve coupled calibrations for each FA or two representative activities FAl and FA consisting in an incremental sub-maximal power specific activity, with EE-HR (heart-rate) relationship determination in laboratory and S-HR and F-HR relationship in the field. These relationships, the physical fitness characteristics and three orthogonal area references are introduced in a mathematical model which calculates efficiency functions S-EE and F-EE. Thirdly, a video recording of the tested activity is achieved with a high-fixed camera, the coordinates of which are introduced in the software. Fourthly, the time events and the coordinates of the image by image tracking of the subject center of mass are stored and transformed to give real in the field coordinates, S, F, aerobic and anaerobic EE of each FA. This method, applied in numerous activities to prepare and drive competitions and records, is the only one to furnish, without strain or traumatic risks for the subjects, a good estimation of anaerobic metabolism and a mean of prevention for deleterious activities.

Enlargement of glycogen store in the rat liver and muscle by a sucrose-diet and exercise training. N. El Elj, B. Mornagui, N. Gharbi, S. El Fazâa (Laboratoire de Physiologie des Agressions, Faculté des Sciences de Tunis, Campus Universitaire, 1060 Tunis, Tunisia).

Glycogen in the liver and skeletal muscle is known to be important to maintain physical performance during prolonged exercise. The purpose of this study was to investigate the effect of long-term intake of a sucrose-diet and exercise training on glycogen content in the liver and skeletal muscle in male rats. Thirty-two rats (130–150 g) were divided into two dietary groups and were fed with a control diet or sucrose diet (containing 20% starch) for 4 wk. During this period, one-half of the rats in each dietary group were trained by swimming exercise (60 $min.day^{-1}$, $5days.wk^{-1}$). The liver glycogen was increased by intake of a sucrose-diet and exercise training ($P < 0.5$).The glycogen content in skeletal muscle showed the same trend as that in the liver. Glycemia does not change in all groups. These results indicate that both long-term intake of the sucrose diet and exercise training synergistically increased glycogen in both tissues.

Normal physical fitness in IDDM adolescent girls despite alteration of sympatho-adrenergic response to incremental exercise testing. E. Heyman, A. Gratas-Delamarche, D. Briard, P. Berthon, S. Vincent, H. Youssef, M. DeKerdanet, P. Delamarche (Laboratoire Physiologie Biomécanique Exercice Musculaire,

UFRAPS, Université Rennes 2, Av. Charles Tillon, CS 24414, 35044 Rennes, France).

An impaired sympatho-adrenergic response to hypoglycaemic episodes has been described in young insulin-dependent diabetic (IDDM) patients, but it is unknown if this altered response occurs with exercise, and if it could influence physical fitness. In this study, plasma epinephrine, norepinephrine and glucose were monitored, via an intravenous catheter, at each stage of a graded exhaustive exercise in 19 post-menarcheal well-controlled IDDM girls (13.3–18.2 years) and 19 healthy siblings. Exercise testing allowed to determine peak $\dot{v}o_2$ and PWC_{170}. Catecholaminergic response was altered in the IDDM girls: norepinephrine levels were significantly depressed at rest and exercise while epinephrine levels were significantly higher at rest and light workloads (< 84 ± 4 W) in the IDDM vs. healthy girls. Plasma glucose remained stable in the healthy girls, whereas it diminished significantly (–6.2 ± 1.3%) throughout exercise in the IDDM girls. However, no relationship was detected between the glucose decrease and the catecholamine increase. The altered catecholaminergic response was not accompanied by physical fitness impairment, since peak heart rate (188.1 ± 2.3 vs. 188.0 ± 2.1 bpm), peak $\dot{V}O_2$ (45.0 ± 1.2 vs. 46.2 ± 1.5 $mL.min^{-1}.kg$ lean-body-$mass^{-1}$) and PWC_{170} (2.41 ± 0.12 vs. 2.64 ± 0.08 W.kg lean-body-$mass^{-1}$) were similar in the IDDM and healthy girls. In addition, the regression of heart rate against workload was comparable in both groups. Nevertheless, the heart rate/norepinephrine ratio was significantly higher at rest and during exercise in the IDDM girls. This study confirms an early sympatho-adrenergic alteration during intense exercise in IDDM girls, but without any implications on physical fitness or cardiac response. Thus an increase in tissue sensitivity to sympathetic drive could be assumed in young IDDM patients.

Effects of prolonged mechanical ventilation on antioxidant systems in the piglet diaphragm. S. Jaber, M. Sebbane, C. Koechlin, M. Hayot, X. Capdevilla, J.J. Eledjam, C. Prefaut, M. Ramonatxo, S. Matecki (EA 701, Laboratoire de Physiologie des Interactions, Muscles et Pathologies Chroniques, 34000 Montpellier, France).

Prolonged controlled mechanical ventilation (PCMV) is known to induce diaphragmatic oxidative stress that seems to be an important factor reducing force generating capacity. In order to better understand the cellular mechanisms involved, the aim of this work was to determine the effect of PCMV on antioxidant defense in the diaphragm with a prospective, randomised, controlled animal study. Eleven piglets (15–20 kg) were assigned to one of two groups: a PCMV group (n = 6) ventilated for three days and a short controlled mechanical ventilation group (SCMV) (CTR; n = 5) ventilated for 3 h. Force frequency curves of the trans-diaphragmatic pressure (Pdi) were obtained in vivo by phrenic nerve pacing. Oxidative stress was evaluated by thiobarbituric reactive substance (TBAR) content and the enzymatic antioxidant activity of both superoxide dismutase (SOD) and glutathione peroxidase (GPx) in samples of diaphragm. Pdi decreased in the PCMV group by 30–35% over the three days at all frequencies. Diaphragm TBAR content was significantly higher and SOD activity was lower in PCMV animals than in control animals after 72 h. GPx activity tended to be lower in the diaphragms of PCMV animals, but this difference was not significant. This study shows that three days of MV in piglets is associated with a decrease in antioxidant activity which could emphasise oxidative stress and both contribute to the diaphragm dysfunction caused by MV.

Effect of prior heavy intensity exercise on the phase II VO_2 kinetics after training. A. Marles, R. Legrand, N. Blondel, P. Mucci, S. Perrey, F. Prieur (Laboratoire d'Analyse Multidisciplinaire des Pratiques Sportives, Université d'Artois UFRSTAPS de Liévin, chemin du Marquage, 62800 Liévin, France).

It has been shown that metabolic acidosis at the onset of exercise can speed VO_2 kinetics by a greater O_2 availability (due to acidosis-induced vasodilatation and the Bohr effect). The aim of this experimentation was to evaluate (1) whether training induced a reduction

of lactic acidosis at the onset of a heavy exercise preceded by heavy-intensity warm up and (2) if this reduction affected the phase II VO_2 kinetics. Eleven sedentary subjects performed tests on a cycle ergometer before and after six-weeks of interval training at 120% VO_{2max}. The test was composed of two 6-min bouts of constant work rate exercises (at 50% Δ ventilatory threshold –VO_{2max}) separated by 6 min at 35 W. This test was performed twice and data were averaged and fitted. The time constant (τ) of the phase II VO_2 kinetics during the first bout was not altered by training (pre-training: 27.2 ± 6.7 vs. post-training: 23.6 ± 9.0 s; NS). Training significantly diminished the blood lactate accumulation at the onset of the second bout (pre-training: 6.2 ± 1.9 vs. post-training: 4.2 ± 1.8 mmol.L^{-1}; $P = 0.01$) while τ of the phase II VO_2 kinetics of the second bout was not significantly affected by training (pre-training: 26.0 ± 5.4 vs. post-training: 26.6 ± 5.9 s; NS). In conclusion, τ of the second bout was not longer after training while blood lactate accumulation was decreased, this may suggest that metabolic acidosis did not influence the phase II VO_2 kinetics. However, this unchanged VO_2 kinetics may be due to not important enough residual effects with training on local vasodilatator to modulate O_2 delivery.

Influence of pattern life on the results of six-minute walk test. K. Masmoudi, S. Aouicha, H. Fki, M. Ketata, N. Zouari (Functional Exploration Department, Bourguiba University Hospital, 3029 Sfax, Tunisia).

To study the effect of socio-economic conditions, educational level and physical activity degree on the results of the six-minute walk test (6 min WT). One hundred fifteen-five voluntary normal subjects (75 female) aged 54.95 ± 0.87 years were studied. Anthropometric and pattern life parameters of each subject were noted. Two 6 min WT were carried out successively with a 30 min interval between them in a hospital corridor on a way of 30 m length in the afternoon. American Thoracic Society recommendations were respected. The parameters studied during 6 min WT were distance covered, heart rate as well as dyspnoea level evaluated by the analogical visual scale. The distance covered was better at the second 6 min WT for all subjects (509 ± 83 m vs. 542.7 ± 89.6 m; $P < 0.001$). Significant correlations were found between distance covered (m) and sex (M: 584(3); F: 498(3); $P < 0.001$), age ($r = -0.47$; $P < 0.001$), IMC ($r = -0.40$; $P < 0.001$), origin (urban: 566.2 ± 9; rural: 513.5 ± 10; $P < 0.001$), education level (illiterate: 483.1 ± 9, primary: 572.7 ± 9, secondary: 600.9 ± 16.3; superior: 638.3 ± 17.6; $P < 0.001$) and physical activity degree (weak: 454.9 ± 8, average: 550.1 ± 7, high: 633.5 ± 9; $P < 0.001$). In conclusion, living conditions must be taken into account when interpretating the 6 min WT.

Effect of a low exercise intensity on mdx hindlimb muscle. S. Matecki, J. Gayraud, A. Cochen, K. Lamber, C. Koechlin, M. Ramonatxo (EA 701, Laboratoire de Physiologie des Interactions, Muscles et Pathologies Chroniques, 34000 Montpellier, France).

Dystrophic muscle training induces beneficial and deleterious effects according to exercise intensity with unknown cellular mechanisms. The aim of the study was to assess the effects of voluntary wheel running exercise on (a) in vivo contractile properties, (b) enzymatic activities and (c) oxidative stress on the tibialis anterior of the mdx mouse, a model of Duchenne muscular dystrophy (DMD). Eighteen mice, aged 8 months old, were randomised into two groups. The training group had free access to voluntary wheel running for 6 weeks. The control group was maintained in a reduced area and was considered as sedentary mice. The tibialis anterior of trained mdx mice showed higher maximal tetanic tension (71.4 ± 4.2 vs. 59.5 ± 3.7 g, $P < 0.05$) and higher specific tension (12.2 ± 0.06 vs. 10.5 ± 0.09 N.cm^{-2}, $P < 0.05$) in vivo than sedentary mice in vivo. However, exercise had no effect on the fatigability of the muscle. Moreover, The activity of citrate synthase (24.0 ± 0.4 vs. 24.4 ± 0.4 μmol.mn^{-1}.g^{-1}) and lactate dehydrogenase (403 ± 32 vs. 404 ± 17 μmol.mn^{-1}.g^{-1}) was unchanged. Lipid peroxidation evaluated by malondialdehyde concentration (MDA), which

is an indirect index of oxidative stress was increased in the training group (131 ± 10 vs. 94 ± 3 μmol.g^{-1}, $P < 0.05$) compared to the control group. The activity of glutathion peroxidase, an antioxidant enzyme, did not change after exercise (7.09 ± 0.7 vs. 5.9 ± 0.3 μmol.mn^{-1}.g^{-1}). In conclusion, low intensity exercise induced in the tibialis anterior of mdx mice, a beneficial effect on force production in spite of any change in fatigue resistance or oxidative metabolism and an increase in oxidative stress.

Prevalence of exercise-induced bronchospasm in basketball players in a hot/humid environment. F. Messan, J. Lounana, J. Medelli (Unité de Biologie de l'Effort et de Médecine du Sport, CHU Amiens, place Victor Pauchet, 80054 Amiens Cedex 1, France).

Several studies have shown that exercise-induced bronchospasm (EIB) is higher among winter sport athletes. Thus, dry, cold air is the strongest triggering mechanism of EIB. To investigate whether regular training in a tropical climate (ambient temperature 26 °C–39 °C; relative humidity 38%–80%) has a possible effect on EIB, we studied 20 young 19.3 ± 1.59-year-old basketball players in Cotonou (Benin). A questionnaire evaluated asthma history and common symptoms of EIB. A calibrated portable spirometer Pony Graphic® (Cosmed, Italy) was used on the field to assess lung function. Spirometry was performed at rest and 5, 10, 15, 20 and 25 min after a specific exercise. Then, an ethnic correction factor was applied to all spirometry data. A fall in FEV_1 of at least 11% was used to evaluate EIB$^+$ and athletes who did not meet this criterion were grouped as EIB$^-$. No significant difference was noticed between groups concerning anthropometric, training data and predictive values. Clinical symptoms were reported in 12/20 subjects (60%) and EIB$^+$ in 7/20 (37%). This last value is much higher than the one of the general population (4%–20%). None of the EIB$^+$ group's value matched with ATS/ERS asthma criteria at rest. Postexercise variation from the baseline in FVC, FEV1 and PEF were significantly different between EIB$^-$ and EIB$^+$ respectively: 15 ± 17% vs. 18 ± 10%, ($P = 0.001$); 13 ± 16% vs. 17 ± 6%, ($P = 0.003$) and 7 ± 17% vs. 11 ± 9%, ($P = 0.023$). FEV1/FVC, FEF25-75 and MEF25 were not different. This study shows that EIB is also induced in hot/humid conditions and its prevalence is the same as the one described in other studies carried out in continental climates.

Effect of mode of recovery on the performance after supra-maximal intermittent exercises. I. Miladi, A. Temfemo, S. Mandengué, S. Ahmaidi (EA 3300: APS et Conduites Motrices: Adaptations-Réadaptations, Faculté des Sciences du Sport, 80025 Amiens, France).

The efficiency of the recovery mode is currently a butt of criticism for it could vary the performance after the intermittent efforts. Nevertheless, stretching turns out to contribute to a better muscular elasticity and blood irrigation, which could also influence recovery. The aim of this study was to determine the effect of the mode of recovery on performance after supra-maximal intermittent exercises. Nine subjects took part in this study. They made three courses of intermittent exercises using three randomised modes of recovery: passive (RP), active (RA) and stretching (RS). The intermittent test consisted in doing two series of four repetitions at 120% MAP during 30 s alternated with a 30-s rest period. The mode of recovery was modified between the 4 min series. After the second series and the 4 min of recovery, the subjects performed a Tlim (maximum time) at 120% MAP until exhaustion. The VO_2 and the FC were recorded by a K4b2. The results demonstrate that the longer length of the Tlim was obtained after an RS ($P < 0.05$) but no difference compared with RA. An increase of peak FC and VO_2 in both series was observed. However, a significant difference in VO_2 peak was found between RA and RP ($P < 0.05$) as well as RS and RP. Besides, the VO_2 peak developed during RS was lower compared to RA and RP, though a longer Tlim was performed during RS. This could be explained by an increase in the nervous activity (EMG) of the muscle and an important lactate elimination during RS. However, no significant difference was observed in VO_2 peak during Tlim.

Muscle oxygenation and blood volume during the Wingate anaerobic test. W. Moalla, G. Dupont, S. Berthoin, S. Ahmaidi (Faculté des Sciences du Sport, 800250 Amiens, France).

The purpose of this investigation was to study the time course of near infrared spectroscopy (Nirs) parameters during a 30-s Wingate anaerobic test (WAnT). Twelve male subjects (24.4 ± 3.9 years; 175.6 ± 6.4 cm; 71.2 ± 6.9 kg; and 16.3 ± 4.1% fat) performed a 30-s WAnT on a cycle ergometer (Monark 814E, Sweden). Peak power, mean power and fatigue index (FI) were calculated. Blood lactate concentration [La] was determined 3-min after the test. Respiratory gas exchanges were measured breath-by-breath using a K4b^2 device. Muscle oxygenation (MO_2) and blood volume (BV) were assessed continuously by Nirs (Runman, USA) on the vastus lateralis muscle. An arterial occlusion was applied immediately at the end of the test to determine changes in MO_2. Mean peak power, mean power and an FI were 850 ± 129 W, 644 ± 73 W and 46.7 ± 17.3%, respectively. $\dot{V}O_{2peak}$ measured at the end of the WAnT was 46.1 ± 6.2 mL.min^{-1}.kg^{-1}. No changes in BV were found between resting and end exercise values. MO_2 decreased progressively and significantly from the beginning until the end of the 30-s WAnT ($P < 0.01$). The decline rate of oxygenation calculated was 0.89 ± 0.23%/s. The latter was significantly related to the $\dot{V}O_{2peak}$ ($r^2 = 0.86$, $P < 0.001$). In contrast, no significant relationship was found neither between MO_2 and FI nor between MO_2 and performance (peak and mean power). These results indicate that BV was not affected during supramaximal exercise and that muscles use oxygen store from the beginning even during anaerobic exercise. Finally, peripheral muscle oxygen consumption measured by Nirs reflect systemic oxygen uptake.

Exercise ventilatory constraints in prepubescent trained children. C. Nourry, F. Deruelle, C. Fabre, G. Baquet, F. Bart, J.M. Grosbois, S. Berthoin, P. Mucci (Laboratoire d'Analyse Multidisciplinaire des Pratiques Sportives, Université d'Artois, chemin du Marquage, 62800 Liévin, France).

We studied mechanical ventilatory constraints in 13 endurance-trained (Tr) and 11 untrained (UT) prepubescent children by plotting the exercise flow-volume (FV) loops within the maximal FV loop (MFVL) measured at rest. The MFVL allowed to determine forced vital capacity (FVC) and maximal expiratory flows. Expiratory and inspiratory reserve volumes relative to FVC (ERV/FVC and IRV/FVC respectively) were measured during a progressive exercise test until exhaustion. Breathing reserve (BR) and expiratory flow limitation (expFL), expressed in the percentage of V_T and defined as the part of the tidal breath meeting the boundary of the MFVL, were measured. Higher FVC and maximal expiratory flows were found in Tr than UT ($P < 0.05$) at rest. Our results have shown that during exercise, except in one subject, all Tr regulated their V_T within FVC similarly during exercise, by breathing with low lung volume at the beginning of exercise followed by breathing with high lung volume at strenuous exercise. In UT, the breathing pattern was quite heterogeneous. The proportion of children who presented an expFL was nearly the same in both groups (~ 70% with a range of 14% to 65% of V_T) and no significant difference was found during exercise concerning expFL. However, higher ventilation (V_E), ERV/FVC and dyspnea associated with lower BR, IRV/FVC and SaO_2 were reported at Ppeak in Tr than UT ($P < 0.05$). These results suggest that, because of their higher V_E level, trained children presented higher ventilatory constraints than untrained children. These may negatively influence the SaO_2 level and dyspnea during strenuous exercise.

Effect of gender, exercise intensity and exercise duration on lipid oxidation during exercise in overweight subjects. F. Pillard, E. Garrigue, C. Moro, I. Harant, I. De Glisezinski, F. Crampes, D. Rivière (Service d'Exploration de la Fonction Respiratoire et de Médecine du Sport, Hôpital Larrey, 24 chemin de Pouvourville, TSA 30030, 31059 Toulouse Cedex 9, France).

To determine if there is a gender difference in lipid oxidation with exercise and the optimal

exercise intensity to oxidize a larger amount of lipids in overweight subjects. Nine youth healthy overweight male and 9 healthy overweight females were selected (BMI: 27.9 ± 0.4 vs. 27.2 ± 0.5 respectively; ns). On one day, the subjects first performed a 30 min cycling exercise at 30% VO_{2max} (E1-session) followed by a 30 min exercise at 50% VO_{2max} (E2-session). In a second session, they performed a similar E1-session followed by 30 min at 70% VO_{2max} (E3-session). From the gas exchange measurements, the nonprotein Respiratory Quotient (RQ) and the debit of fatty acids mg oxidised.min^{-1}.kg^{-1} lean mass (FAOD/kgLM) were calculated. Plasmatic concentrations (pc) of glycerol and non-esterified fatty acids (NEFA) were assayed. RQ was significantly lower for women only during the E1-session. For both genders, RQ decreased with the duration of exercise during E2 and E3-sessions. During the E1-session, the FAOD/kgLM was higher among women and it did not change over time despite the pcNEFA being increased. FAOD/kg LM was higher during the E2-exercise. During E2 and E3-sessions, the FAOD/kgLM was increased as the exercise time was prolonged (over 10 and 20 min) simultaneously with the increasing of the pcNEFA. In conclusion, lipid oxidation during exercise is optimised for middle-intensity exercise and long exercise. The lack of lipid mobilization would be an essential factor that would limit lipid oxidation in middle and high-intensity exercises.

Effect of prior heavy exercise on pulmonary O_2 uptake and muscle oxygenation. F. Prieur, A. Marles, R. Legrand, N. Blondel, P. Mucci (Laboratoire d'Analyse Multidisciplinaire des Pratiques Sportives, UFR STAPS, chemin du Marquage, 62800 Liévin, France).

Purpose: pulmonary O_2 uptake (VO_2) and muscle oxygenation were examined during two bouts of heavy cycling exercise in young healthy subjects. Methods: ten young males performed two constant work rate exercises of six minutes (at 50% Δ ventilatory threshold – VO_{2max}) separated by 6 min at 35 W. VO_2 was measured breath by breath and muscle oxygenation of the right vastus lateralis was monitored by NIRS and was expressed in % according to the ischemia-hyperemia scale (Muscle oxygenation = Mox%). The changes in VO_2 (i.e. the VO_2 slow component) and in Mox% during each bout were evaluated as the difference between the 6th and the 3rd minute of exercise ($\Delta VO_{2(6'-3')}$ and $\Delta Mox_{(6'-3')}$). Results: VO_2 was not different at the end of each bout of exercise (bout 1: 2320 ± 339 mL.min^{-1} vs. bout 2: 2316 ± 371 mL.min^{-1}, *NS*) and Mox% was significantly higher at the end of the second bout (31.1 ± 6.3%) in comparison with the first one (24.8 ± 6.5%, $P < 0.001$). $\Delta VO_{2(6'-3')}$ was significantly reduced by prior exercise (187 ± 66 ml.min^{-1} vs. 94 ± 69 mL.min^{-1}, $P < 0.001$) whereas $\Delta Mox_{(6'-3')}$ was not significantly altered by prior exercise (bout 1: –0.7 ± 2.9% vs. bout 2: –1.1 ± 1.5%, NS). Conclusion: muscle oxygenation at the end of heavy exercise was enhanced by prior heavy exercise suggesting that muscle O_2 delivery was improved by a vasodilator-induced acidosis effect. Moreover, this study does not support the hypothesis that the VO_2 slow component is associated with changes in muscle oxygenation during exercise since prior exercise decreased $\Delta VO_{2(6'-3')}$ but did not alter $\Delta Mox_{(6'-3')}$.

SaO_2 is normalised during aerobic exercise in hypoxemic obese adolescents. J.M. Sène, M.L. Frelut, G. Pérès (Physiologie du Sport, CHU Pitié-Salpètrière, AP-HP75013 Paris, CTP Margency et Hôpital St-Vincent-de-Paul AP-HP 75014, Paris, France).

Aerobic conditions are very important to maintain and improve during physical training in obese subjects. Blood oxygen saturation (SaO_2) was measured during an aerobic exercise performed in agreement with current recommended physical activities for obese adolescents. SaO_2 was measured on arterialised blood (GEM Premier 3000® analyser) in 19 sedentary obese (38.5 ± 5.4 kg.m^{-2}) adolescents (13.9 ± 1.5 y) during a rectangular exercise performed on a cycle ergometer (Monark 824E®). The test included 4 successive phases: T1 at rest (5 min), T2 at 50% VO_{2max} (10 min), T3 at 70% VO_{2max} and T4 at recovery (5 min). Expired gases were analysed (Schiller-Medisoft®) and heart rate

was recorded (Polar®). SaO_2 increased significantly during exercise between T1 (93.7% ± 1.6) and T2 (95.3% ± 1) or T3 (94.9% ± 1.3) and remained stable at T4 (94.8% ± 1.5). These variations are fitting corresponding changes in PaO_2 at T1 (65 ± 6 mmHg), T2 (74 ± 5 mmHg), T3 (77 ± 6 mmHg) and T4 (74 ± 8 mmHg). The ventilatory stimulation obtained by stimulation of exercise leads to a significant ($P < 0.01$) increase in SaO_2 and PaO_2, reflecting improved alveolar ventilation. In conclusion, Well-designed rectangular aerobic exercise is able to restore better oxygen flow in obese adolescents.

Contribution of oxidative stress in unloaded–induced skeletal muscle atrophy: prevention by vitamin E supplementation. S. Servais, R. Favier, M.H. Mayet-Sornay, C. Duchamp, D. Desplanches (Unité Mixte Recherche 5123 CNRS, Université Claude-Bernard, Lyon, France).

Exposure to reduced activity induces skeletal muscle atrophy. Oxidative stress might trigger muscle wasting. This study was designed to test the hypothesis that long-term supplementation of the lipid-soluble antioxydant vitamin E prior and during the phase of unloading would counteract some of the detrimental consequences in rat soleus muscle. Fourteen days of hindlimb suspension caused a 50% atrophy while with vitamin E the soleus muscle atrophied only by 32%. After suspension, administration of vitamin E partly prevented the loss of type I (–59% vs. –38% for H rats) and IIa (–42% vs. –32% for H rats) fibre size. Supplementation affected neither the decreased ratio of reduced (GSH) vs. oxidised glutathione (GSSG) nor the increased antioxydant enzyme (superoxide dismutase, catalase, glutathione peroxidase) activities observed after unloading. In contrast, vitamin E resulted in increased levels of UCP2 (uncoupling protein) and HSP 72 (heat shock protein) as a complementary protection against oxidative stress and suppressed the increase (+50%) in concentrations of thiobarbituric acid-reactive substance (TBARS) caused by suspension. Our results suggest that oxidative stress contributes to soleus atrophy and vitamin E supplementation partly prevents muscle disuse.

Alteration of the mitochondrial efficiency in non-alcoholic steatohepatitis: a liver adaptation? B. Sibille, C. Romestaing, V. Rouleau, M. Dautresme, I. Ollivier, M. Belouze, B. Rey, S. Servais, C. Duchamp, M.A. Piquet (PICM, UMR5123 CNRS-UCB Lyon 1, France).

The non alcoholic steatohepatitis (NASH) is an emerging pathology associated with obesity and insulin resistance. The causes of NASH and its consequences on liver functions are poorly understood. The aim of this study was to evaluate the modifications of mitochondrial metabolism in rats fed a choline-methionine deficient diet (CMDD), a known model of NASH. Male Wistar rats fed a standard diet or CMDD during 6 weeks. Liver mitochondria respiration and efficiency (ATP/O) were measured. Reactive oxygen species (ROS) production was estimated using a fluorimetric detection of mitochondrial H_2O_2 formation. Lipid metabolism was approached by a measure of ketone body production and oxygen consumption of isolated hepatocytes from fasted rats. Liver triglyceride content (30-fold increase) and histologic analysis confirmed the steatohepatitis in CMDD rats. An uncoupling of the mitochondrial oxidative phosphorylation in CMDD fed rats was demonstrated by an enhanced oligomycin-insensitive respiration (32.2 ± 2.1 vs. 20.0 ± 1.3 nanoatom O/min/mg protein, $P < 0.05$), a decreased mitochondrial efficiency and a reduced ROS production (5.6 ± 2.7 vs. 19.2 ± 4.2 pmoles H_2O_2/nmoles O_2, $P < 0.05$). These results were related to an enhanced (56%) activity of the cytochrome oxidase. An increased lipid oxidation was found in CMDD fed rats as reflected by both a rise in the following: (i) isolated hepatocyte respiration with dihydroxyacetone and octanoate (38.9 ± 4.2 vs. 27.2 ± 2.6 μmoles O_2/unit of citrate synthase) and (ii) ketone body formation (178 ± 19 vs. 139 ± 9 μmoles/unit of citrate synthase). In conclusion, choline-methionine deficient diet fed rats showed a mitochondrial dysfunction suggesting a liver adaptation to the overload of triglycerides and oxidative stress. Indeed, mitochondrial uncoupling increased lipid oxidation and decreased

ROS production. These mitochondrial adaptations could limit NASH-associated injuries.

Effect of endurance exercise on airway cells in runners. Z. Tabka, W. Ben Turkia, I. Ben Cheikh, B. Sriha, A. Zbid, (Service de physiologie et des Explorations Fonctionnelles, Hôpital Farhat Hached, Sousse 4000, Tunisia).

Recent studies have shown that asthma is most commonly found in endurance events, such as cycling, swimming, or long distance-running. There is a high prevalence of asthma and exercise induced bronchoconstriction. A long term effort and resistance in athletes is often associated with symptoms and signs of airway inflammation. The use of induced sputum is a convenient and reliable non-invasive method of assessing airway inflammatory cells. The purpose of this study was to investigate the effect of endurance exercise on total and differential airway cell counts. Ten long-distance runners (19 ± 3 years) and 12 control subjects (20 ± 3 years) were studied. Pulmonary function tests were performed using spirometry. Sputum was induced on two occasions using nebulised hypertonic saline (10%), before and after one hour running at 80% of VO_{2max}. Analysis of induced sputum showed increased cellularity ($P < 0.01$) after the race. Instead the absence of post-race respiratory symptoms or spirometric changes, airway cell counts change significantly: the runners showed increased neutrophil and lymphocyte differential counts in induced sputum ($P < 0.02$). Physical exertion, particularly when intense and prolonged, causes significant stress to the respiratory system. Associated hyperventilation and increased airway exposure to contaminants of inhaled air could explain cellular changes. This study shows an increase in the airway of inflammatory cells, which reflects only a normal response to a supra-physiologic stimulus.

Reduction in spontaneous physical activity level in daily life: possible role in human overweightness. V. Van Wymelbeke, V. Gigot, L. Nataf, D. Rigaud, L. Brondel (Centre des Sciences du Goût, 15 rue Hugues Picardet, 21000 Dijon, France).

The prevalence of overweightness in most affluent countries has increased in recent years and the reduction of physical activity level in daily life could play a major role in this phenomenon. In order to check this hypothesis, 24 men (25.2 ± 1.3 years) differing in their body mass index (lean: 19.2 ± 0.3 $kg.m^{-2}$, normal: 22.5 ± 0.6 $kg.m^{-2}$, heavy: 28.7 ± 0.6 $kg.m^{-2}$) and in their food intake (little eaters: 7361 ± 397 kJ, normal eaters: 9919 ± 242 kJ, big eaters: 12615 ± 731 kJ) were recruited. Food intakes were evaluated by a 7-d food record and controlled during 2 days before the 24 h-session in a calorimetric chamber. Energy expenditure and spontaneous physical activity were measured respectively by indirect calorimetry and by a force plate-form coupled with an accelerometer. The results indicate no difference in energy intakes between the 3 weight groups. Physical activity measured by the force platform is lower and with less variability (SD of accelerations) in the heavy group than in the lean group ($r = -0.445$, $P < 0.05$). Furthermore, lean and big eater subjects have a greater spontaneous physical activity than heavy and little eater ones ($r = -0.410$, $P < 0.05$). In conclusion, this study shows that overweight subjects have a limited spontaneous physical activity (qualitatively and quantitatively) in daily life. Overweight and lean individuals could behave differently; sedentary behaviour could be favoured by overweight subjects.

Oxidative stress and biochemical evolution of professional cyclists during different race types. I. Vouldoukis, G. Peres, G. Guillaume, D. Mazier, M. Conti (Inserm/UMR 511, CHU Pitié Salpétrière, AP-HP, Université Paris VI, 75013 Paris, France).

The aim of this work was to evaluate biochemical and oxidative stress evolution among professional cyclists during intensive exercise. In this way, we chose two different race types, a short and individual against the clock race (A) and a heavy endurance team race (B). Eleven blood parameters allowing oxidative stress exploration and 23 metabolical parameters were followed before and after exercise. The results were strongly different between race type, but

also between racers. During the (A) race, an alteration of antioxidant defences was observed, with an increase in MDA, oxidised glutathion concentrations and glucose-6-phosphate deshydrogenase activity. A strong hyperlactatemia was observed, with a decrease in bicarbonate concentration. Racers implemented their lipidic metabolism, with an intensive lipolysis and induction of ketone bodies. During the (B) race, more pronounced variations of antioxidant defences were observed, like modifications in G6PDH, Cu/Zn SOD, catalase and glutathione reductase activities. Discrete lipolysis was observed – but no ketone mobilisation – and signs of muscular lysis and electrolytic perturbations. However, the biochemical status differed between the racers, with great inter-individual variations and adverse evolutions. In the two types of races, the racers with the best results had the best antioxidant status before races. Moreover, during the (A) race, the best racer did not implement lipidic metabolism. In conclusion, at the end of intensive exercise, antioxidant and biochemical status of professional cyclists depends on the type of race, individual and short, or long and intensive. The initial status seems to be of the major importance to ensure performances.

Obesity among Lebanese adolescents: behavioral factors (physical activity and dietary habits). H. Youssef, C. Jacob, E. Moussa, M. Zind, C. Groussard, A. Delamarche (Laboratoire de Physiologie et de Biomécanique de la Performance Motrice, Université de Balamand, El- Koura, Nord Liban, PO Box, 100 Tripoli, Liban).

Currently, the prevalence of obesity and its related diseases are increasing all over the world and especially in industrialised and developing countries. The latest studies show that this blight is affecting the young population more and more. Lebanon is no exception, it has a growing number of obese and overweight young adolescents. Indeed, Sibaï et al. (2003) reveal that 7.7% of boys and 2.9% of girls aged between 10 and 19 years are obese, and 26.9% and 14.7% of them are overweight. These percentages become reversed at an adult age: females (18.8%), males (14.3%). However, these authors did not explain this paradox. Therefore, the objective of this study was to carry out a survey during adolescence which is a key period concerning morphological changes. Seven hundred forty-five Lebanese adolescents (14–18 y) participated in this study (420 girls, 315 boys). The first results confirmed those of Sibaï et al. (2003) since we reported more obese and overweight subjects in boys compared to girls (9.5% vs. 1.9%) and (22.5% vs. 13.1%). Concerning the behavioral aspect, on the contrary to more industrialised countries, Lebanese overweight and obese boys and girls are more interested in extracurricular physical activities than healthy subjects (in boys: 58.5% vs. 27.5% and in girls: 38.1% vs. 27.5%). However, only 37% of boys and 25.5% of girls questioned, declare that they have breakfast everyday. Therefore, more investigations are needed in their dietary habits in search of reasons for obesity.

Effects of swallowing on central respiratory pattern generator. F. Al Chama, P. Calabrese, G. Benchetrit, P. Baconnier (TIMC-PRETA, Faculté de Médecine de Grenoble, UJF, BP 53, 38041 Grenoble Cedex 9, France).

In order to characterise the interaction between respiration and swallowing and its eventual dysfunctions, we recorded ventilation on 4 healthy subjects (age 25–30, 2 males) during periods with spontaneous (saliva) or provoked (beverage) swallowing. Respiratory signals were obtained by respiratory inductance plethysmography such this is the only measure compatible with drinking and eating. Each swallowing was characterised by its duration and time of occurrence in the respiratory cycle. The effect of swallowing on the respiratory pattern was quantified by the changes induced in the current cycle duration and amplitude, and in the amplitude and inspiratory and expiratory durations of the following cycle. The recorded swallows can be grouped into three categories those which (i) start and end during inspiration, (ii) start and end during expiration and (iii) start in inspiration and end in expiration. The results show the following (i) the duration of swallowing is simply added to the cycle duration

as compared to the preceding cycle and (ii) with regards to the following cycle, the later the swallowing occurs in the cycle the larger the increase in its amplitude. We developed a mathematical model describing the interaction between the central respiratory pattern generator and the mechanical respiratory system, which allows testing the hypothesis that during swallowing, the respiratory centers progress is stopped. An additional hypothesis necessary to explain the increase in the following cycle's amplitude is that during simulated swallowing, the central respiratory pattern generator is progressively moved away from its free-run cyclic trajectory. The three types of observed swallowing, were simulated with our model and the result shows that the model behaves qualitatively (and often quantitatively) similarly to the physiological system.

Effects of fasting at Ramadan on exercise substrate utilisation and insulin sensitivity. I. Aloulou, K. Masmoudi, N. Zouari (Functional Exploration Department, H. Bourguiba Hospital, Sfax, Tunisia).

We evaluated the effects of fasting during Ramadan on Insulin Sensitivity (SI) and substrate utilisation during exercise. Nine voluntary women (age: 40.1 ± 2.3 years; BMI: 26.23 ± 1.2 $kg.m^{-2}$) underwent anthropometric, blood fasting sampling with analysis of Insulinemia (Ib) and Glycemia (Gb) and a metabolic exercise test. This test included 6 min exercise at 20, 30, 40 and 50% of theoretical power and estimated the level of power at which energy derives mainly from glucose oxidation: "Crossover point" and the level of power at which lipid oxidation is maximal "Lipoxmax". All these measures were done during the week before and after Ramadan. Several indexes of SI were calculated: Quantitative Insulin Sensitivity Check Index (QUICKI) = 1/[Log (Ib) + Log (Gb)]; Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) = (Ib×Gb)/22,5; Fasting Insulin Resistance Index (FIRI) = (Gb×Ib)/25; the index SI = 40/Ib; Ib×Gb; Ib/Gb et Gb/Ib. Fasting at Ramadan induces a significant body weight loss (67.3 ± 2.9 vs. 66.2 ± 2.7 kg, $P < 0.05$) with reduction of lean mass (43.9 ± 1 vs. 42.7 ± 1.1 kg, $P < 0.01$) and hydrous mass (32.1 ± 0.7 vs. 31.2 ± 0.7 kg, $P < 0.001$). "Crossover point" and "Lipoxmax" were not altered after one month fasting during Ramadan with respectively 47.1 ± 4.1 vs. 51.2 ± 2.4 watts ($P = 0.7$) and 42.4 ± 5.5 vs. 43 ± 3.3 watts ($P = 0.3$). Insulin sensitivity estimated by simple indexes based on Ib and Gb was not affected by one month fasting during Ramadan. In conclusion, fasting at Ramadan induces a body weight loss without any change on SI or substrate oxidation during exercise.

Variations of the expression of serum Hsp70 and the plasmatic rate of free tryptophan during endurance exercise. A. Amara, I. Mrizak, I. Latiri, Z. Tabka, A. Zbidi (Laboratory of Physiology and Functional Explorations, Faculty of Medicine of Sousse, Av. Med El Karoui, 4000 Sousse, BP 126, Tunisia).

Following physical exercise, several metabolic variations take place on the level of the organism. The objective of this work was to follow the tolerance of the sportsman to endurance exercise according to the expression of serum Hsp70 and the variation of the rate of free tryptophan. We evaluated a group of sportsmen comprising 9 involved subjects of average ages (19.6 ± 0.84 years), sizes (180.5 ± 4.6 cm), weight (75.8 ± 9.04 kg) and VMA (16.5 ± 1.4 $km.h^{-1}$). The experimental protocol consisted in running to 65% aerobic maximum speed during one hour. This test was carried out on a treadmill. Two blood samples were taken before and with the stop of the exercise to analyse the expression of serum Hsp70 and the plasmatic rate of free tryptophan. Our results show a nonsignificant increase (11.56 vs. 12.68 $ng.mL^{-1}$) in the expression of Hsp70 and a light nonsignificant increase in the rate of tryptophan before and after the effort (2.43 vs. 2.68 $\mu mol.L^{-1}$). We note that the exercise was responsible for the release of disturbances which caused the variation of the expression of Hsp70 in various parts of the organism. These disturbances reveal the installation of tiredness confirmed by the increase in the rate of free tryptophan.

Maximal respiratory gas exchange data in young Tunisian athletes: factors of variation and available norms.A. Baklouti, I. Latiri, Z. Tabka, A. Zbidi (Laboratoire de Physiologie et des Explorations Fonctionnelles, Faculté de Médecine de Sousse, Tunisia).

Aerobic physical fitness exploration, in young athletes in the laboratory, is realised during incremental exercise. Representative norms of the population studied are required for maximal respiratory parameter interpretation. In fact, physical fitness assessment, in young athletes, allows the sports federation to elaborate level groups of training, adaptation programs and to authorize demanders of outclassement. The purpose of this study was to determine specific predictive equations of maximal respiratory gas exchange data in relation with anthropometry parameters (age (A), height (H) and weight (W)) in Tunisian young athletes. Seventy-two young athletic boys aged from 9 to 16 years participated in this study. Their height and weight were respectively 155 ± 2 cm and 45 ± 5.6 kg. The subjects performed an incremental maximum exercise test on a bicycle ergometer (Lode, Groningen) with stepwise triangular increasing loads at 60 rotations per minute. Analysis of instantaneous gas exchange was carried out by a breath-by-breath CPX-D/CPX CardiO_2 analysis system (Medical Graphics). Anaerobic threshold (SV_1) was determined by the ventilatory equivalent method. Predictive equations were estimated to use techniques of linear, multiple regressions and the concept of allometric scaling. For statistical analysis, STATISTICA was used. A p-value of less than 0.05 was considered significant. The results show that maximal oxygen consumption, maximal ventilation and anaerobic threshold increased significantly ($P < 0.05$) with anthropometry parameters. The correlation analyses indicate that maximum respiratory characteristics had the strongest correlation with anthropometry parameters ($P < 0.05$). In fact, representative norm utilisation of VO_{2max}, VE_{max} and SV_1 is an indispensable step taken to propose an incremental protocol exercise standardisation.

BDNF participates in the anorexigenic signalling in the dorsal vagal complex. B. Bariohay, B. Lebrun, E. Moyse, A. Jean (Laboratoire de Physiologie Neurovégétative, Université Paul Cézanne Aix-Marseille III-UMR 6153 CNRS–1147 Inra, avenue Escadrille Normandie-Niemen, 13397 Marseille, France).

Brain-derived Neurotrophic Factor (BDNF) has been implicated in the central control of food intake, acting as an anorexigenic factor. Whereas BDNF and its receptor TrkB are expressed in the hypothalamus and in the dorsal vagal complex (DVC), the two main centres involved in food intake control, previous works have been focused on the hypothalamus as a probable site of action for this neurotrophin. In the ventromedial hypothalamus (VMH), BDNF expression is regulated by the nutritional state and is a downstream effector of melanocortin signalling. In this study, we addressed whether, in adult rats, the DVC can be considered as a second site of action for the BDNF anorexigenic effects. For this, we measured: (i) the effect of intraparenchymal infusion of exogenous BDNF (provided by Regeneron) within the DVC on food intake and body weight; and (ii) the endogenous BDNF protein content in the DVC and the hypothalamus, after food deprivation or peripheral treatments by the anorexigenic hormones leptin (provided by Amgen) and cholecystokinin (CCK). BDNF infusion within the DVC induced anorexia and weight loss. Moreover, in the DVC, BDNF protein content was down-regulated after food deprivation and up-regulated by leptin. CCK induced a transient up-regulation of BDNF protein content, first in the DVC and later in the hypothalamus. These results constitute the first demonstration that BDNF exerts an anorexigenic effect in the DVC. Since CCK was recently shown to stimulate melanocortin signalling within the DVC, a tempting hypothesis is that in this structure, as in the VMH, BDNF could be a downstream effector of melanocortin signalling.

Imaging of regional lung ventilation in mice using Xe-enhanced quantitative synchrotron radiation computed tomography (SRCT). S. Bayat, S. Monfraix, L. Porra, C. Nemoz, G. Berruyer, W. Thomlinson, P. Suortti, A.R.A. Sovijärvi (European Synchrotron Radiation Facility, BP 220, 38043 Grenoble, France).

We recently introduced a respiration gated Xe-enhanced SRCT technique that combines excellent spatial resolution with the ability to both visualize and directly quantify inhaled stable Xe gas used as a tracer, by K-edge subtraction (KES) imaging (Bayat S, Le Duc G, Porra L et al., Phys. Med. Biol. 2001, 46: 3287–3299). Since KES uses x-ray beams with narrow energy bands, sufficient flux is available only with high-intensity synchrotron sources. In the present study, the experimental setup was miniaturized, and imaging spatial resolution was improved using a low-noise fast-readout (FRELON) CCD camera (pixel size = 49 μm). Experiments were performed in 1 anaesthetized and mechanically ventilated C57BL/6j mouse. A detailed description of the KES method can be found elsewhere (Bayat, Le Duc, Porra et al., Phys. Med. Biol. 2001, 46: 3287–3299). Measurements of regional ventilation were based on kinetics of Xe wash-in. Single high-resolution Xe-KES tomograms were acquired using the FRELON camera. A map of regional specific ventilation (min^{-1}) was obtained, based on single compartment model curve fitting, and determination of Xe wash-in time constants. This technique allows functional lung imaging in small animals with quantitative lung ventilation measurements. Further study will allow application in small animal models of obstructive lung diseases.

Study of fenugreek- seed- extracts on cholesterol and triglyceride levels in cholesterol fed rats. O. Belguith Hadriche, K. Jamoussi, A. Feki, F. Makni Ayadi (Laboratoire d'Écophysiologie Animale, Faculté des Sciences de Sfax, BP 802, 3018, Tunisia).

Fenugreek (*Trigonella foenum graecum*) is known for its pharmacologic and nutritional properties. In previous studies, fenugreek-seed elicited a reduction in plasma of lipid levels. The aim of this study was to investigate the effects of fenugreek extracts in cholesterol fed rats. Rats were divided into 8 groups as follows: control, cholesterol fed group, cholesterol plus fenugreek fed group and 5 groups fed cholesterol with different extracts of fenugreek (1/ethyl acetate, 2/dichloro-methane, 3/hexane, 4/methanol and 5/water). Blood samples were obtained to analyse cholesterol levels (CT) and triglycerides (TG). Plasma concentration of cholesterol was increased in the cholesterol fed group and in the groups fed cholesterol with dichloro-methane extract, hexane extract, methanol extract and water extract. However, a decrease in CT and TG was found in those treated with cholesterol plus fenugreek and cholesterol plus the ethyl acetate extract from fenugreek. These results suggest that ethyl acetate extract from fenugreek seed opposed to the hypercholesterolemic effect of a cholesterol enriched diet.

Beneficial effect of IGL-1, a modified UW solution, on a liver graft after prolonged cold ischemia. I. Ben Mosbah, H. Ben Abdennebi, D. Saidane, K. Ben Mosbah, J. Roselló-Catafau, C. Peralta (Department of Experimental Pathology, Institute of Biomedical Investigations CSIC-IDIBAPS, Barcelona, Spain).

The hypothermic storage of livers remains the major approach to human liver preservation because low temperature decreases the metabolism of preserved organs. The University of Wisconsin (UW) cold storage solution has been introduced to decrease ischemic graft damages. Several studies have demonstrated that it is possible to improve cold-preservation solutions modifying the UW solution composition: the simple inversion of K^+ and Na^+ concentration and the substitution of hydroxyethyl starch, one of the UW solution components, by polyethylene glycol (PEG) in UW (IGL-1 solution) improves rat liver and kidney function. The present study was performed to assess the effect of the new preservation solution: IGL-1, manufactured by the Institute Georges Lopez (Lyon, France) and a standard UW solution on liver damage after prolonged cold ischemia (24 h). In order to evaluate the effectiveness of IGL-1 cold storage solution in liver injury, AST and ALT were measured. To appraise the severity of liver injury after 24 h of cold ischemia, hematoxylin and eosin-stained sections were evaluated by a point- counting method on an ordinal scale. The results showed that the use of the IGL–1 preservation solution significantly

reduced hepatic damages, evidenced by decreased AST and ALT levels in the flash effluent at the end of the preservation period. Liver histological findings after cold storage revealed a disintegration of hepatic cords when the UW solution was used; on the contrary, with the IGL-1 solution the integrity of the hepatic cords was maintained. This study demonstrates the superiority of the IGL-1 solution to protect liver grafts against prolonged ischemia damage; this might be of interest in improving hepatic graft viability in liver transplantation.

Trimetazidine protects the rat liver against cold ischemia injury. I. Ben Mosbah, D. Saidane, H. Ben Abdennebi, J. Roselló-Catafau, C. Peralta (Departamento de Patología Experimental, Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC), Rosselló 161, 08036 Barcelona, Spain).

Liver transplantation has become a well-established procedure for therapy of fatal liver diseases. In spite of dramatic improvements in this procedure and its outcome, preservation injury, occurring during cold ischemia and subsequent reperfusion, is still considered to be a crucial factor for graft outcome in organ transplantation. In this context, preservation solutions are one of the master keys to improve the organ quality after the preservation period. The present study was performed to assess the effect of trimetazidine (TMZ, 10^{-6} M), an antioxidant agent, added to a UW solution on liver damage after prolonged cold ischemia. Livers preserved for 24 h in UW solution with and without TMZ were then flushed with 50 mL of Ringer lactate. Aliquots of the effluent flush were sampled for AST and ALT measurements, the effect of TMZ on ATP level after cold storage was also evaluated. Hematoxylin and eosin-stained sections were evaluated by a point- counting method on an ordinal scale. The results showed that TMZ in UW significantly reduced hepatic damage, evidenced by decreased AST and ALT levels in the effluent. Higher ATP was observed when TMZ was added to the UW solution. Liver histological findings revealed a disintegration of hepatic cords when the UW solution was used; on the contrary, by TMZ addition, the integrity of hepatic cords was maintained. These findings suggest that TMZ addition in UW solution could be a relevant new strategy to protect against cold ischemia damages that might be of interest in improving hepatic graft viability in liver transplantation.

Hepatotoxicity of hexachlorobenzene (HCB) in *Meriones shawi shawi* (Gerbillidae). S. Ben Romdane, A. Sellami (Laboratoire de Physiologie Animale, Faculté Sciences Tunis, Campus Universitaire, 2092 El Manar, Tunis, Tunisia).

HCB is an organochlorinated pesticide which belongs to the family of persistent organic pollutants (POP). Used for a longtime as a fungicide in agriculture, its utilization was stopped in 1972. However, it continues to be produced as an unintentional by-product in the manufacturing of chlorinated solvents. With its resistance to environmental degradation and its mobility, HCB is widely distributed throughout the world and even in Tunisia. Many epidemiologic studies have shown the dangerous effects of HCB on living creatures. The aim of this work was to evaluate the effects of a subacute exposition of HCB on the body weight and liver of a desert rodent, *Meriones shawi shawi*. Females Meriones were submitted to gavage with the doses of 0 mg (control group), 0.16 mg, 4 mg and 16 $mg.kg^{-1}$ b.w./day during 30 days. Our results show a significant decrease of the body growth in the three treated groups. The liver weight was not affected with 0.16 and 4 $mg.kg^{-1}$ b.w./day of HCB; a significant increase was observed with the highest dose (16 mg). The hepatic glycogen stores were reduced with the treatment in all treated groups. The histological structure of the liver was altered by HCB showing vacuolization of the cytoplasm being more important with the dose of 16mg. These results reveal a hepatotoxicity of these low doses of HCB in this species.

Maximal anaerobic power is not altered by prior exercise with a different muscle group. E. Bouhlel, S. Chelly, I. Mrizak, Z. Tabka (Unité de Recherche, Institut Supérieur du Sport et de l'Éducation Physique, Kef, Tunisie).

The aim of this study was to examine whether blood lactate production at the end of a force-velocity test with legs contributed to a reduction of the maximal anaerobic power (W_{max}) performed with arms. Seven well-trained subjects (age: 20 ± 2, height: 181 ± 7 cm, weight: 86 ± 14 kg) performed two protocols that consisted of two consecutive force-velocity tests with legs and then with arms: (i) Arm cranking force-velocity test (A1) followed by leg cycling force-velocity test (L2). Eight minutes rest separated A1 and L2. (ii) Leg cycling force-velocity test (L1) followed by arm cranking force-velocity test (A2) on a Monark cycle ergometer (type 894 E). Eight minutes rest separated L1 and A2. Blood lactate value at rest averaged 1.6 ± 0.3 mmol.L^{-1}. Blood lactate concentrations after A1 and L2 were 6.8 ± 1.4 and 6.2 ± 1.8 mmol.L^{-1} respectively. Blood lactate after L1 and A2 were 5.7 ± 1.3 and 6.5 ± 1.5 mmol.L^{-1} respectively. The prior force-velocity test with legs did not alter the following maximal anaerobic power performed with arms and vice versa: W_{max}-A1 and W_{max}-A2 were 594 ± 126 W and 581 W ± 145 respectively (NS); W_{max}-L1 and W_{max}-L2 were 1041 ± 283 W (12 ± 2.6 W.kg^{-1}) and 1081 ± 353 W (12.6 ± 3.2 W.kg^{-1}) (NS). In conclusion, the repetition of 6 to 8 sprints during a force-velocity test (Vandewalle, 1986) with legs involve blood lactate production. However, this production does not alter the W_{max} performed with arms. Maximal anaerobic power is not altered by prior exercise with a different muscle group. The force-velocity test with legs and with arms could be used consecutively in the laboratory to evaluate the W_{max} in trained athletes.

Expression of extracellular matrix components and their integrin receptors in the adult rat adrenal gland. S. Campbell, M. Otis, N. Gallo-Payet, M.D. Payet (Département de Physiologie et Biophysique, Faculté de Médecine et des Sciences de la Santé, Université de Sherbrooke, 3001, 12^{e} avenue, Sherbrooke, Québec, Canada).

The binding of integrins to extracellular matrix (ECM) components triggers intracellular pathways that are involved in adhesion, migration, proliferation and cell survival. We used immunohistochemistry and indirect immunofluorescence techniques to investigate the presence of ECM components and integrins in the adult rat adrenal glands. We showed that collagen type I was expressed in the adrenal capsule, was found as short fibrils in the adrenal cortex and was present around adrenal medulla cells. Collagen type IV staining was found in the zona glomerulosa and as long fibrils throughout the cortex with a weak labeling in the capsule. Laminin and fibronectin were both expressed in the capsule and in the zona glomerulosa with fibrils entering the inner zones of the cortex. Like collagen I, collagen IV, fibronectin and laminin staining was also observed around cell clusters of the medulla labeled with anti-dopamine beta hydroxylase antibody. Integrin subunits $\alpha 1$ showed a strong labeling in the adrenal medulla with a weak staining in the cortex. The $\alpha 2$, $\alpha 3$ and $\alpha 5$ showed strong staining in the adrenal cortex with some cells labeled in the medulla. Integrin subunits $\alpha 8$ and $\beta 1$ were detected throughout the adrenal gland with no specific expression pattern. Localization of ECM components and their associated integrins provide important information to understand specific function related to each zone of the adrenal cortex, like proliferation and aldosterone secretion in the zona glomerulosa or migration and secretion of corticosterone in the zona fasciculata.

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Ubiquitin/proteasome pathway as an early protective mechanism against hyperoxia in the airway. A. Chambellan, S.A. Comhair, K.A. Szabo, P. Cruickshank, P. MacKenzie, S.C. Erzurum (Institut du Thorax, CHU Nantes, 44093 Nantes Cedex 1, France).

Human bronchial epithelial cells are vulnerable to hyperoxia and fail to increase the primary intracellular antioxidant enzymes such as superoxide dismutases, catalase or glutathione peroxidases. Because of this inability to enhance an appropriate antioxidant response against hyperoxia and the accumulation of oxidatively modified proteins in bronchial

epithelial cells, we postulate that other protective mechanisms involved in protein degradation, e.g. the ubiquitin-proteasome pathway, may have a central role at the early phase to maintain the homeostasis of the epithelial layer. In order to evaluate the first events to the adaptive response to hyperoxia, we examined gene expression of bronchial epithelial cells by using a large scale microarray approach. We analysed the mRNA levels of human bronchial epithelial cells in 8 healthy volunteers obtained from brushing at bronchoscopy before and after 12–16 h exposure to > 95% O_2. We describe the genes modulated by hyperoxia gaining insights into the underlying biological altered functions. The processes involved confirmed the ubiquitin dependent protein catabolism pathway to be the main early response to hyperoxia. Because of the few numbers of subjects enrolled in the study and the individual polymorphism in gene expression causing variability, we confirmed our results by using human bronchial epithelial cells (BET-1A) exposed to > 95% O_2 in an in vitro study. Our findings indicate that protein processing and catabolic pathways, which are critical for preventing accumulation of oxidised and/or misfolded proteins in the cells, are involved in the early response of the airway epithelium to oxidative stress.

Low-voltage electrical stimulation improves blood flow and enhances angiogenesis in ischemic rat skeletal muscle. P. Dobšák, M. Nagasaka, J. Siegelová, J. Jančík, J.-C. Eicher, JE. Wolf, K. Imachi, M. Kohzuki (Department of Functional Diagnostics and Rehabilitation, St. Anna Faculty Hospital Brno, Faculty of Medicine, Masaryk University, Pekařská 53, 656 91 Brno, Czech Republic).

Electrical stimulation of the skeletal muscle has been reported to promote vascular endothelial growth factor (VEGF) production but induction of angiogenesis in the muscle by low-voltage electrical stimulation (LVES) is not fully understood. This study was designed to assess the effects of LVES on blood flow restoration in ischemic skeletal muscles, and to investigate whether LVES-induced VEGF is due to the hypoxia or inflammation by measuring hypoxia-inducible factor (HIF-1α) and interleukin (IL-6). In-vivo experiments of hind limb ischemia (with bilateral excision of femoral arteries) were conducted on male Sprague-Dawley rats (n = 7). A stimulating electrode was implanted into the right tibialis anterior muscle (RTAM); the left one (LTAM) served as a control. Continuous LVES was maintained for 5 days (frequency 25 Hz; voltage 0.1 V; 24 h/day). Then, the evaluation of blood supply in RTAM and LTAM was done using laser-Doppler imagery (the results are expressed in relative units – RU); VEGF concentrations from muscle samples were determined by the ELISA assay, and the levels of HIF-1α and IL-6 by immunohistochemical staining. Five days of LVES significantly increased blood supply in RTAM (489.3 ± 61.5 RU vs. LTAM 348.7 ± 32.6 RU; $P < 0.0277$), and also the VEGF production in stimulated RTAM (131.7 ± 9.6 ng.L^{-1} vs. LTAM 110.3 ± 9.6 ng.L^{-1}; $P < 0.01$). No significant differences were observed in tissue levels of HIF-1α and IL-6 in stimulated or non-stimulated TAM. In conclusion, continuous LVES in skeletal muscles could be effective in angiogenesis enhancement and blood supply restoration, and could have an important therapeutic value in ischemic vascular diseases.

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Rugby practice and skeleton: correlations between strength, BMD and biochemical markers of bone remodeling. M. Elloumi, D. Courteix, S. Sellami, Z. Tabka, G. Lac (LPPM, Université Clermont II, 63177 Aubiere, France).

This study reports observed correlations between muscular strength, bone mineral density (BMD) and content (BMC), biochemical markers of accretion (osteocalcine) and resorption (C-telopeptide or CTx) in rugby players. Twenty male rugby players of the Tunisian rugby team (25.6 ± 0.8 years, 178.3 ± 1.3 cm, 92 ± 3.3 kg, 17.1 ± 1.3% LBM); Strength measurements: handgrip + Bosco mat; BMD: double X ray absorptiometry; Biochemical markers dosage: Emethods. Positive significant

correlations ($P < 0.001$) were shown between strength and total and regional (rachis, legs, femoral neck which are specifically stressed by this sport practice) BMD. In the same way, the osteocalcin, but not CTx, was highly correlated with the same regional BMD and total BMD. In a previous study, we show that rugby players present higher BMD and BMC than sedentary people, and among rugbymen, that forwards particularly had higher BMD than backs, on account of impact number and struggle phases they have to sustain (Elloumi, Courteix, Sellami, Tabka, Lac, Int J Sports Med 2006 (in press)). This study was done to verify if strength characteristics might be correlated to biochemical markers of bone metabolism. It appears that the muscular strength, which is itself correlated to the lean body mass, is a major determinant of the skeleton quality. Moreover, the correlation reported between the BMD and the osteogenic marker osteocalcin, suggests that this positive bone adaptation may be linked to an improvement of the bone remodelling speed.

Progressive isometric strength training restores endothelial function in ovariectomized female rats. H. Figard, V. Gaume, F. Mougin, A. Berthelot (Laboratoire de Physiologie, Faculté de Pharmacie, place Saint Jacques, 25030 Besançon Cedex, France).

Exercise training enhances vasodilation via augmented endothelial release of nitric oxide (NO). Ovariectomized rats develop a typical endothelial dysfunction resembling that observed in postmenopausal women. The aim of this study was to investigate whether a progressive isometric strength training protects against endothelial dysfunction induced by estrogen deficiency in female rats, as efficiently as 17β-estradiol. Twenty-four female Sprague-Dawley rats (4 weeks old) were subjected to a bilateral ovariectomy (OVX). Eight sham operated animals (SHAM OVX) served as the control. After surgery, the animals were randomly assigned to one of the four treatment groups for 14 weeks as follows: (i) a sedentary control group receiving subcutaneous (s.c.) daily injection of 17β-estradiol 20 $\mu g.kg^{-1}$ (OVX SED17β); (ii) sedentary control group receiving daily vehicle s.c. (OVX SED); (iii) progressive isometric strength training group (every morning, 5 days/week), receiving daily vehicle s.c. (OVX ISO); (iv) sedentary sham operated group (SHAM OVX). Endothelium response was evaluated with cumulative concentrations of acetylcholine (ACh 10^{-10}–10^{-5} M) in aortic rings precontracted with norepinephrine (10^{-7} M). The concentration-response curves for ACh demonstrated that ACh-induced vasodilation was enhanced in aortic rings obtained from the OVX ISO group, as evidenced by the highest pD2 value (7.77 ± 0.11) compared to OVX SED (7.17 ± 0.14) and SHAM OVX (7.24 ± 0.09) groups. 17β-estradiol treatment increased endothelium-mediated vasodilation in OVX SED17β compared to OVX SED rats, however exercise training significantly improved endothelial function to a greater extent as compared to 17β-estradiol. The present results show, that isometric strength training is associated with improvement of ACh-induced vasodilation in ovariectomized female rats. The ability of physical activity to counteract endothelial dysfunction suggests its potentially useful role in the prevention of cardiovascular diseases.

The results of a food consumption survey carried out in French high level rugby players. J. Finaud, M. Elloumi, F. Maso, H. Vidalin, A. Robert, G. Lac (BAPS, Biologie B, Les Cézeaux, 63177 Aubière, France).

The objective of this study was to evaluate the dietary intake in high level rugby players (n = 26, 26.9 ± 2.9 years, 185.9 ± 8.7 cm, 98.9 ± 13.9 kg, 16.6 ± 2.4% MG) according to the seven-day dietary intake method and to compare the results with the allowed standard values. The global caloric intake (3267 ± 636 $kcal.d^{-1}$) was in agreement with the RDA. At the qualitative level, the same bias as for the sedentary populations might be noted: too low complex carbohydrates and polyunsaturated free fatty acids, too many lipids, particularly saturated free fatty acids, monounsaturated free fatty acids and cholesterol. The ratio of proteins and micronutrients seem adequate for this population even if certain subjects show deficit

signs in magnesium, calcium, zinc, and in vitamins D or C. Correlations were shown between fat-mass and global caloric intake ($P < 0.001$) and more particularly between the fat mass and global lipid ($P < 0.05$), saturated fatty acid ($P < 0.05$), and cholesterol ($P < 0.001$) intakes. Since the fat mass was itself negatively correlated with VO_{2max} ($P < 0.001$), it may be postulated that these dietary bias impact negatively on physical performance. Thus, the rugby players will probably draw benefits of some nutritional advice for their health and sport performance.

The anthropometric index, lipid metabolism and insulinoresistance index in the glucose intolerance. A. Ghouini, K. Khelfat (Laboratoire de Physiologie, Faculté de Médecine de Blida, 9000 Blida, Algeria).

This work was aimed at appreciating the obesity incidence (by means of body mass index "BMI" and waist/hip ratio "WHR"), by fasting blood lipoproteins, glucose and insulin during the glucose intolerance. Blood lipoproteins, glucose and insulin dosage, as well as the calculation of the glucose/insulin "G/I" relationship (insulin resistance index) were effected in normal, glucose intolerant obese and glucose intolerant normal weighed subjects (20 subjects in each group). At the end of this study, it was clear that insulin resistance is shared in an almost equal way in glucose intolerant obese subjects and in normal weighing ones. The two factors which are charged in insulin resistance (BMI and WHR) did not show in our study any relationship with insulin resistance in glucose intolerants classified according to their "BMI" or "WHR". However, the VLDL and LDL concentrations were elevated in obese subjects. It is possible that lipid metabolism and insulin resistance index are not associated perhaps for many nutritional and metabolic reasons.

Altered antioxidant status in spontaneously-hypertensive rats fed a fructose-enriched diet.A. Girard, S. Madani, F. Boukortt, J. Belleville, J. Prost (UPRES Lipides et Nutrition, 6 boulevard Gabriel, 21000 Dijon, France).

High fructose doses mainly consumed in industrial countries have been shown to induce metabolic abnormalities such as hyperinsulinemia, insulin resistance, dyslipidemia, clustered as syndrome X. The changes in antioxidant defense are unknown in hypertension associated with metabolic disorders induced by a high fructose diet. Twenty spontaneously hypertensive rats (SHR) were divided into 2 groups. The fructose-fed animals received a fructose-enriched diet (60% fructose) while control animals received a control diet containing starch (60%). After a 13-week-diet period, the total antioxidant status was performed in blood and liver by monitoring the rate of free radical-induced RBC hemolysis (KRL^{TM} test). Lipid peroxidation was assessed in plasma, the VLDL-LDL fraction and liver as the production of thiobarbituric acid reactive substances (TBARS). Antioxidants (enzymes and vitamins) were determined respectively, in blood or plasma and in the liver. Compared with controls, rats fed the fructose diet showed similar blood pressure but hyperglycemia and plasma hyperinsulinemia. The fructose diet increased both plasma and VLDL-LDL TBARS concentrations and decreased liver TBARS levels. In the fructose group, Cu/Zn-SOD and GSH-Px activities were significantly lowered in erythrocytes whereas they were increased in the liver. The non enzymatic defense system was also affected in the plasma of the fructose group, by increased ascorbic acid levels and decreased α-tocopherol and retinol concentrations. Feeding a fructose-enriched-diet negatively affects the antioxidant capacity in the blood of hypertensive rats, but it has no deleterious effect on the liver suggesting a better defense in this organ.

Determinants of membrane factor (Dm) and capillary lung volume (Vc) in healthy subjects. S. Glénet, C. de Bisschop, R. Dridi, H. Guénard (Laboratoire de Physiologie EA 518, Université Bordeaux 2, Faculté des Sports de Poitiers, France).

The main determinants of Dm and Vc in healthy subjects were analysed using the NO/CO method (Guénard et al., Respir Physiol 1987, 70: 113–120). Twenty-five subjects 24 to

63 years old, 20 men and 5 women, were included in the study. Maximal oxygen consumption was measured as well as Dm and Vc with a Medisoft equipment (Dinant, Belgium). Several measurements were performed at total lung capacity (TLC) as well as at 65 and 80% TLC. Measurements were also performed during positive (+12 h Pa) or negative pressure (–9 h Pa) breathing. Vc in standard condition at TLC depends on lung volume, age and oxygen consumption $Vc = (33.6 + 12) \times VA - (0.9 \times \text{âge}) + (0.7 \times VO_{2max})$ ($r = 0.9$; $P < 0.05$). The main determinant of Dm was the lung volume. Dm increased by 58% between 65 and 100% TLC, as the increase in Vc was meaningless. Positive pressure breathing decreased Vc slightly as negative pressure breathing increased Vc significantly from 115 to 126 mL. The relationship between Dm and lung volume was not linear, of the type $Dm = 24.6 \times V_L^{0.8}$ ($r = 0.96$), suggesting that the lung neither behaves like a bellow, in which case the relation would be linear, or like a simple bubble in which case the exponent of the relationship would be 0.67. Dm and Vc appeared very sensitive to different physical determinants which could associate their effects in physiological situations such as change in position or muscular exercise.

Chromosomal damage in turbot (*Scophthalmus maximus*) exposed to fuel oil. Comparison of two contamination protocols. C. Goanvec, T. Lacoue-Labarthe, H. Ollivier, M. Theron, K. Pichavant, E. Poirier, S. Le Floch, J. Laroche, V. Maxime, L. Nonnotte, G. Nonnotte (Unité de Physiologie Comparée et Intégrative, UFR Sciences et Techniques, 6 Av. le Gorgeu CS 93837, 29238 Brest Cedex 3, France).

Turbots (*Scophthalmus maximus*), were exposed to fuel oil number 2, either intraperitoneally (with two doses) or with contaminated water. Biliary metabolites were evaluated by fixed fluorescence to verify the efficiency of intoxication. EROD activity was compared to chromosomal damage measured by flow cytometry. Biliary metabolite analyses showed a good dose/response relation and constituted a clear reference for the subsequent measurements. Comparing flow cytometry and EROD results, a shorter delay of response for EROD activity was obtained. The persistence of EROD response was shorter while the genotoxic signal still persisted after one month. The measurement of chromosomal damage allowed a good differentiation between the two tested doses; in the case of EROD activity, the results were less clear. These results suggest that within a few weeks, after exposure to fuel oil number 2, the measurements of chromosomal damage by flow cytometry can be used to detect a dose dependant genotoxic response in fish.

Superoxide dismutase activity in macrosomic newborns. O. Grissa, A. Kasdallah-Grissa, M. Jebi, A.H. Miled, M. Bibi, Z. Tabka (Service de Physiologie et des Explorations Fonctionnelles, Hôpital Universitaire Farhat Hached, 4000 Sousse, Tunisia).

Low birth weight has appropriately been the focus of extensive health policy and research endeavours, but high birth weight, also associated with adverse maternal and infant outcome, has received less focus inquiry. The purpose of this preliminary study was to evaluate the oxidative stress in macrosomic newborns and their mothers. Superoxide dismutase levels as an indicator of oxygen radical activity were determined in both maternal and umbilical cord blood. The comparison was made between macrosomic newborns ($n = 20$) with mean weight 4330 ± 0.05 g, size 48.65 ± 0.43 cm and cranial perimeter 34.05 ± 0.23 cm and normosomic newborns ($n = 20$) who weighed 3120 ± 0.10 g, and have 49.33 ± 2.34 cm of size and 35.58 ± 0.29 cm of cranial perimeter. The same comparison was made between their mothers. Our results showed that erythrocyte SOD activity was significantly reduced ($P < 0.01$) in macrosomic babies (452.21 ± 67.43 $U.g^{-1}$ Hb) when compared with the control babies (1159.10 ± 114.91 $U.g^{-1}$ Hb). The maternal levels of SOD showed the same result with mean values about (646.21 ± 76.69 $U.g^{-1}$ Hb) in women who had macrosomic babies and (1405.00 ± 202.00 $U.g^{-1}$ Hb) in the control women. The percentage decreases in SOD levels were 70% and 54% for babies and mothers, respectively. We note that enzyme activity

is significantly lower ($P < 0.05$) in cord blood samples than the maternal values in both macrosomic cases and controls. Decreased activity of the enzyme scavenger, superoxide dismutase, which catalyses the dismutation of $O_2^{\cdot-}$ into H_2O_2 indicates a deficiency in the antioxidant defence system during macrosomia and the implication of oxidative stress. Based on these findings, it is speculated that foetal macrosomia is associated with alteration in antioxidant status in babies and their mothers. This parameter has the potential to show the efficacy of using antioxidants such as vitamin E and/or vitamin C to reduce oxidative stress in macrosomic babies and the risk of foetal and maternal complications.

The effects of TRH in the adult male rat. F. Hadj-Bekkouche, R. Djediat, A. Naroun (LBPO, Endocrinologie, Faculté des Sciences Biologiques, USTHB BP 32 El Alia Bab-Ezzouar, Alger, Algeria).

TRH has been isolated from the mammalian hypothalamus. It plays a central role in regulating the pituitary thyroid axis. The purpose of this study was to examine the effects on the thyroid axis and the genital system. Two doses were used, 200 $\mu g.mL^{-1}$ and 250 $\mu g.mL^{-1}$, and injected intraperitoneally. The duration of the treatment varied from four to eight days. The Wistar rats were divided into three groups: group 1 ($n = 16$) received 250 $\mu g.mL^{-1}$ for four days, group 2 ($n = 8$) 200 $\mu g.mL^{-1}$ for eight days and group 3 ($n = 15$) 250 $\mu g.mL^{-1}$ for eight days. Two control groups were considered in each group, one (C, $n = 5$) without injection and the other (T, $n = 5$) received the same volume of the vehicle (NaCl‰). All the animals were weighted daily. The body weight increased significantly ($P < 0.001$) with TRH 200 $\mu g.mL^{-1}$ and 250 $\mu g.mL^{-1}$ ($P < 0.05$) for eight days. FT3 increased significantly ($P < 0.02$) compared to control C and reduced significantly ($P < 0.02$) compared to control T. Plasma testosterone concentration showed a significant decrease ($P < 0.05$). The follicular epithelium of the thyroid was significantly ($P < 0.001$) reduced. The average height of the epididyme appears to be significantly ($P < 0.001$) lower than the control 1 and 2. The results indicate that TRH increases body weight. This effect may be due in part to GH. Moreover, it reduces plasma testosterone and this is probably involved in the decrease of the epithelium of the epididyme. On the thyroid axis, TRH might reduce the effects of stress.

Low calorie-diet and ageing. K. Hamden[a], A. Elfek[a], S. Carreau[b] ([a] Écophysiologie Animale, Faculté de Sciences, Sfax, Tunisia; [b] Biochimie, USC Inra, Université, Caen, France).

The time effect on living organisms shall be considered at various stages from the molecular level to the whole individual and the society. Following the free radical theory [Harman, 1956], numerous works have been published dealing with the deleterious effect of oxygen and oxidative processes on molecular ageing especially on the cell membrane. The aim of this work was to analyse the putative relationship between diet energy and ageing. Male Wistar rats aged of 5 months were bred under the same conditions with free access to a pellet diet. Three groups ($n = 8$ per group) of animals were studied: a control group (C) with a diet of 335 $kcal.day^{-1}.kg^{-1}$ body weight, a group (R1) receiving 248 kcal and a third group with the lower calorie-diet (R2) of 165 kcal. These treatments were performed during 6, 7, 9, 10 and 12 months. Among the different parameters measured during the study, only data related to malonedialdehyde (MDA) are presented. Indeed, it is well known that MDA is a good marker of cell membrane damage following ROS production during stress. In the control group, MDA levels increased by 50% in the liver between 6 and 12 months (12–24 $nmol.g^{-1}$, respectively), 44% in the spleen (24–42 $nmol.g^{-1}$), 20% in the kidneys (40–50 $nmol.g^{-1}$) and 29% in the testes (11–15 $nmol.g^{-1}$). In the group R1, the MDA levels increased but much lesser than in the control group (–20% for the liver; –11% in the spleen; 63.6% in the kidneys and –20% in the testes compared to MDA in untreated animals). In the animals fed with the lowest energy diet, the MDA levels were similar to those of the control group. Consequently, we may conclude

that a low calorie diet (R1) without changing the quality of the pellet and which does not induce a starving behavior (R2) is likely suitable to protect against (lower MDA level) or delay the apparition of cell membrane damage consecutive to ageing in the male rat.

Effects of atherogenic diets in *Psammomys obesus*. N. Hamlat, S. Neggazi, Y. Benazzoug, G. Kacimi, S. Chaïb, S. Aouichat-Bouguerra (Nutrition and Metabolism laboratory, FSB, USTHB, PO Box 32, 16111 El Alia, Algiers, Algeria).

Since vascular complications often accompany diabetes, *Psammomys obesus* is a model of human nutritionally induced diabetes when transferred from its native halophilic plant nutrient to the standard laboratory diet, inappropriate to their metabolic capacity. In order to compare the effects of two atherogenic diets and the nutritional interaction, three groups of Psammomys were exposed to a six month protocol: a natural diet (20–22 cal.day^{-1}); natural diet and 1/4 egg yolk (40 cal.day^{-1}); standard laboratory diet and 1/4 egg yolk (52.5 cal.day^{-1}). Hyperglycemia and hypertriglyceridemia were more pronounced in animals maintained on halophilic plant and egg yolk than in Psammomys maintained on a standard diet and egg yolk; a marked hypercholesterolemia characterised the two groups receiving egg yolk (superior to 1500 mg.dL^{-1}). Hyperproteinemia appeared at the second month of experimentation and was more pronounced in Psammomys on a naturel diet with egg yolk. A high level of production of atherogenic lipoproteins (VLDL-LDL) and a decrease of antiatherogenic fractions (HDL) were registered in the two groups of experimental Psammomys. At autopsy, the hepatic content indicates that the increase of total lipid in Psammomys on a halophilic plant diet with egg yolk is more important (296%) than in Psammomys on a standard laboratory diet with egg yolk (110%); the reason for each histology showed that the hepatic steatosis was more pronounced in the first group. The histological examination of the thoracic aorta showed important alteration in two groups of Psammomys on an atherogenic diet (blood aggregation, proliferation and migration of smooth muscle cells, collagen accumulation and elastolysis) but the dramatic effects were only revealed after the administration of halophilic plant with egg yolk (a cut of the aortic segment).

Interactions of caloric restriction with cytotoxic effects of nickel chloride in stress protein expression in rats. N. Hfaiedh, M.S. Allagu, F. Croute, J.P. Soleilhavoup, A. El Ffeki (Laboratoire Écophysiologie Animale, Faculté des Sciences de Sfax, BP 802, 3018, Tunisia).

Nickel and Ni compounds are well recognised carcinogens. Indeed, increased risks of lung and nasal cancers have been detected in people working in Ni industries. It is suggested that the $NiCl_2$ induced toxicity might be mediated by generation of H_2O_2 and/or by induction of the Fenton reaction which generates hydroxyl radicals. Recently, low amounts of reactive oxygen species (ROS) were detected in A549 cells exposed to $NiCl_2$ (250–1000 μM) for 45 min (Salnikow et al., 2000). An over expression of specific stress proteins such as heat shock proteins (HSP) was shown to follow the accumulation of misfolded proteins in cells. HSP are known to act as molecular chaperones to restore the correct folding of damaged proteins. They are also crucial in reinstalling cellular homeostasis. The present study deals with the effects of Ni on the expression level of the cytosolic HSP72/73 and the reticulum-associated GRP94. Experiments were carried out on Wistar female rats (3 months old, 130 g body weight) who were randomly divided into two batches: the normally fed (N) batch was given 20 g of food pellets per animal daily. The animals submitted to diet restriction (J) were given the same amount of food pellets 1 day over two. After one month, each batch was divided into two groups. The animals were injected daily, for 10 days, with either 4 mg.kg^{-1} body weight $NiCl_2$ or with the same volume of saline solution. Another set of experiments were carried out using cell lines derived from the human lung (A549). The cells were cultured for 4 days in the permanent presence of 100, 200, or 400 μM $NiCl_2$. The Ni induced over

expression of HSP73 and GRP94 in the kidneys of rats and in A549 lung cells. In this respect, the important lowering of the HSP72 we observed under our experimental conditions in the kidneys of rats and in the cell lines is puzzling and the mechanism underlying this effect is still speculative. No such effect was observed in the kidneys of rats submitted to intermittent fasting in stress proteins. This could be related to the fact that nickel was shown to generate reactive oxygen species and caloric restriction was associated with a decrease of free radical generation.

Improvement of regional blood supply by electrical stimulation of strength muscles in patients with end-stage congestive heart failure. J. Jančík, P. Dobšák, J. Siegelová, H. Svačinová, J. Vítovec, P. Balcárková, L. Kožantová, J.C. Eicher, J.E. Wolf (Department of Functional Diagnostics and Rehabilitation, St. Anna Faculty Hospital Brno, Faculty of Medicine, Masaryk University, Pekařská 53, 656 91 Brno, Czech Republic).

This study was designed to investigate the influence of low-frequency electrical stimulation [LFS] of strength muscles on regional blood flow in patients with advanced form of congestive heart failure [CHF]. Fifteen patients with CHF [mean age 51.5 ± 7.2 years, class NYHA III-IV, mean EF 19.8 ± 3.5%] underwent 6-week stimulation training using LFS (frequency 10 Hz; amplitude 60 mA; 60 min/day; 7 days.week^{-1}) applied simultaneously to quadriceps and calf muscles of both legs. Blood flow velocity (BFV) of the right femoral artery and cardiac output (CO) were measured at the baseline and at the end of the training period by pulsed-wave Doppler velocimetry and by trans-thoracic echocardiography. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were monitored during each period of stimulation [in 15-min intervals]. Six weeks of LFS significantly increased the mean blood flow velocity in the right femoral artery compared to the value at the baseline (48.2 ± 4.1 cm.s^{-1} vs. 35.6 ± 3.9 cm.s^{-1}; $P < 0.05$). There were no significant differences in the values of CO measured at the baseline and at the end of the training period; the measurement of SBP, DBP and HR did not show any significant changes during the stimulation. In conclusion, long-term regular application of LFS of strength muscles could improve the blood supply in stimulated muscles in patients with CHF. The results presented also demonstrate that LFS is a safe and well-tolerated method, without life-threatening side effects.

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Physical activity and obesity in Down syndrome. S. Joffroy, S. Geneau, A. Durieu, S. Garnier, S. Lemoine, P. Mauriège (UFR-STAPS, Université de Toulouse III, 118 Route de Narbonne, 31062 Toulouse Cedex, France).

The prevalence of overweight and obesity in Down syndrome was investigated in 578 children and adults living in different communities in France. Body Mass Index (BMI) and its relations with selected anthropometric measures, environmental factors as dietary habits and physical activity were determined. Males (45.4%) and 61% females were categorised as overweight and obese according to the classification of OMS (1998). The middle BMI in our population was more important than that observed in the French population (25.4 kg.m^{-2} vs. 24.4 kg.m^{-2}), and was always higher in women than in men, irrespective of age (26.9 ± 6.7 kg.m^{-2} for females vs. 24.5 ± 4.9 kg.m^{-2} for males, $P < 0.05$). The middle BMI increased with age from 41–50 years and decreased after 60 years. Physical activity alone had a great influence on BMI, irrespective of the volume and type of activity (endurance, or not). Even if the cause of obesity in people with Down syndrome is unknown but is probably multifactorial, it may involve poor eating behavior, calorie intake, depressed metabolic rate, reduced exercise, hypotonia and endocrine abnormalities. In conclusion, our results show physical activity induces an important reduction of BMI in the Down syndrome population. Other investigations should be considered when studying the course of this pathology.

Respiratory muscle oxygenation kinetics: relationships with breathing pattern. R.

Legrand, F. Prieur, A. Marles, C. Nourry, N. Blondel, S. Lazzari, P. Mucci (Laboratoire d'Analyse Multidisciplinaire des Pratiques Sportives, UFR Staps, chemin du Marquage, 62800, Liévin, France).

We purpose to investigate respiratory muscle oxygenation kinetics monitored by NIRS and to study relationships with breathing parameters, in young healthy subjects, during exercise. Nineteen young males performed a maximal incremental test on a cycle ergometer to determine maximal oxygen consumption (VO_{2max}), and to locate changes in the breathing pattern by studying the VO_2 corresponding to an accelerated rise in breathing frequency (F_{bacc}), plateau of tidal volume ($Vt_{plateau}$) and inflection point in the VE/Vt relationship ($VE/Vt_{inflection}$). First and second ventilatory threshold (VT1 and VT2) were also determined. Respiratory muscle deoxygenation (RMD) kinetics were monitored by NIRS. $\dot{V}O_2$ at which RMD was accelerated (RMD_{acc}) and the amplitude of RMD at maximal exercise (ΔOXY) were determined. All subjects showed significant RMD. VO_2 corresponding to RMD_{acc} and to change in breathing pattern were not different. Relationships were found between the VO_2 corresponding to RMD_{acc} and the VO_2 corresponding to Fb_{acc} ($r = 0.88$, $P < 0.001$), $Vt_{plateau}$ ($r = 0.84$, $P < 0.001$), $VE/Vt_{inflection}$ ($r = 0.58$, $P < 0.05$) or VT2 ($r = 0.79$, $P < 0.001$). ΔOXY was related to VO_{2max} ($r = 0.58$, $P < 0.05$). In conclusion, RMD_{acc} seems to be due to the change in breathing pattern and especially to the important rise in breathing frequency at this intensity level, i.e. VT2. Moreover, subjects who exhibit higher VO_{2max} also exhibit higher RMD. This supports the hypotheses that (i) respiratory muscle oxygenation participates significantly in total VO_2 during strenuous exercise (ii) the respiratory muscle share of whole body VO_2 becomes more elevated as the level of aerobic fitness increases.

Outlow tract obstruction during exercise in hypertrophic cardiomyopathy impaired primary hemostasis. T. Le Tourneau, S. Susen, A. Millaire, A.S. Polge, C. Caron, N. Lamblin, P. de Groote, G. Deklunder, C. Bauters, B. Jude (Inserm ERI-9, EA 2693, University of Lille, Service d'EFCV, Hôpital Cardiologique, Bd Pr J. Leclercq, 59037 Lille Cedex, France).

Outflow gradient in hypertrophic cardiomyopathy (HCM) might impair primary hemostasis with Willebrand factor (VWF) proteolysis. The magnitude of the outflow gradient may vary with numerous physiological alterations. In HCM, we sought to evaluate (i) the relationships between outflow gradient and VWF impairment, and (ii) the effect of exercise on gradient and VWF. Thirty-five patients (44 ± 16 y) with either obstructive (HOCM, 6) or non obstructive (HCM, 29) hypertrophic cardiomyopathy underwent a semi-supine symptom-limited exercise echocardiography (EE). Selected parameters reflecting VWF abnormalities were evaluated under basal conditions and within 1 h after EE. Outflow gradient increased significantly with EE (13 ± 13 to 42 ± 47, $P = 0.0001$). Under basal conditions, shear-induced platelet adhesion (PFA 100®) was prolonged in HOCM compared with HCM (264 ± 55 vs. 150 ± 55%, $P < 0.0001$). VWF-collagen binding activity (VWF:CB) and the percentage of high molecular weight multimers (% HMW) of VWF were significantly reduced in HOCM compared with HCM (59 ± 18 vs. 113 ± 49%, and 4.8 ± 1.3 vs. 11.0 ± 1.9% respectively, $P < 0.0001$). There was no change in % HMW after EE, but a slight decrease of PFA 100® and an increase in VWF:Ag and VWF:CB (all $P < 0.05$). There was a strong correlation between either PFA 100® or % HMW at rest and the maximal value of peak gradient during EE ($r = 0.72$ and $r = -0.76$ respectively, $P < 0.0001$). The peak gradient during EE was the only independent predictor of hemostasis alteration at rest. In conclusion, obstruction in HOCM leads to an impairment of primary hemostasis. Primary hemostasis impairment at rest is highly predictive of the maximal value of peak gradient during exercise.

Effect of exercise on non-enzymatic antioxidant status in professional cyclists. J. Medelli, J. Lounana, J.J. Menuet, F. Messan, Z. Cordero-MacIntyre (CHU Amiens, Amiens, France).

The objective is to evaluate the impact of maximal short duration exercise on oxidative stress and the relationship between the plasma antioxidant status, serum lipid radical levels and aerobic performance. Twenty-four professional male cyclists performed incremental exercise on a bicycle ergometer until exhaustion. Cu, Zn, Se, α-tocopherol,VitA, β-carotene and Thiobarbituric Acid Reactive Substances (TBARs) were measured before/after exercise. Hgb and Hct were measured to calculate plasma volume change. The non-parametric Wilcoxon test was used for comparison before/after exercise and the Spearman test was used for correlations. Values of $P < 0.05$ are significant. At rest, plasma concentrations of Vit A, α-tocopherol, β-carotene and Se are higher than normal in 75, 54, 32 and 61% of the subjects. TBARs are positively correlated with VO_{2max} ($r = 0.44$) and anaerobic threshold VO_2 ($r = 0.49$), Zn and Se with anaerobic threshold power ($r = 0.41$ and 0.40). There was a significant drop in Vit A ($P < 0.05$), β-carotene ($P < 0.05$), α-tocopherol ($P < 0.01$) and Se ($P < 0.01$) but no change in Zn, Cu and TBARs after adjustment for plasma volume change after exercise. Change in Vit A was positively correlated with power and all biological parameters (except TBARs). In conclusion, these results show a decrease of non-enzymatic antioxidants after exercise and suggest an improved anti-oxidant status induced by training.

Expression of Hsp70 in the serum and in mononuclear cells and modification of the physiological parameters during endurance exercise. I. Mrizak, F. Slama, I. Ben Cheikh, W. Ben Turkia, Z. Tabka, A. Zbidi (Laboratory of Physiology and Functional Explorations, Faculty of Medicine of Sousse, Av. Med El Karoui, 4000 Sousse, BP 126, Tunisia).

The study sample was composed of two groups: trained and sedentary subjects. The protocol of effort comprised two visits: the first was the determination of maximum oxygen uptake. The second visit was that of a rectangular test to follow the tolerance to endurance exercise (one hour of running with 65% of the maximum oxygen consumption) of the two groups according to the expression of Hsp70 in systemic circulation and the mononuclear cells of blood. Besides Hsp70, other biochemical parameters (lactic acid, creatin phosphokinase CPK, urea) were analysed during the second visit. The first visit indicated that the trained subjects had a level of activity definitely higher than that of the sedentary subjects. The second visit showed that the trained group presented biochemical disturbances due to a peripheral tiredness expressed by higher rates of lactic acid at rest compared to the sedentary subjects. In addition, the rates of CPK were maintained high, exceeding the standards all along the second visit. This unexpected particular situation of the subjects involved seems to influence the expression of serum and mononuclear Hsp70, which resulted in higher rates in the latter compared to the sedentary subjects. So serum and mononuclear Hsp70 of blood can be a tool for the early detection of peripheral tiredness, before the subject reaches the symptoms revealing a confirmed installation of tiredness which can lead to a fall of performance.

Bone mineral density in young Tunisian soccer players. A. Nebigh, H. Rebai, M. Elloumi, Y. Trabelsi, I. Tarhouni, Z. Tabka, S. Sellami (Laboratory of Physiology and Functional Explorations, Faculty of Medicine Sousse, Tunisia).

We purpose to evaluate the effect of the practice of soccer on bone mineral density during growth in prepubertal boys. Forty-eight subjects, prepubertal boys (Tanner stage (2–4) at the start of the study), took part in this study. A series of 25 young soccer players (age: 13.1 ± 0.3 y) trained from 8 to 10 h per week. The control group was formed of 23 subjects (age: 12 ± 3.7 y) and did not practise any extra scholar sport. The proportion of CTX (cross labs resorption marker) was carried out by an immunological technique. The body composition, bone mineral density (BMD) and bone mineral content (BMC) were measured by dual energy X-ray absorptiometry (DEXA). Concerning the parameters of body composition, we did not find a difference between young soccer players and the controls.

The tendency observed between the values of CTX for soccer players (2.26 ± 0.52 ng.mL^{-1}) and controls (2.14 ± –0.69 ng.mL^{-1}) was not significant. However, the values of BMD were significantly higher in the soccer players compared with those of the controls. The same significance was verified for values for whole body BMC ($P < 0.001$). In conclusion, these results suggest that soccer, which is a weight bearing physical activity, has a beneficial effect on bone content and density acquisition especially during growth.

Experimental hypothyroidism and aortic alterations in *Psammomys obesus*. S. Neggazi, N. Hamlat, Y. Benazzoug, M. Ardjoun, S. Chaïb, S. Aouichat-Bouguerra (Nutrition and Metabolism laboratory, FSB, USTHB, PO Box 32, 16111 El Alia Algiers, Algeria).

Atherosclerosis pathogenesis is complex because of its multifactorial characteristic. Hypothyroidism is one of the factors implicated. For our study, we used 2 groups of animals: *Psammomys obesus* and *Rattus norvegicus*. In each group, rats were rendered hypothyroid by addition of 0.03% of Carbimazole/day/animal to their drinking water during a period of 5 months in *Psammomys obesus* and 11 months in *Rattus norvegicus*; control rats were given plain water. Hypothyroidism estimated by TSH measurement performed on *Rattus norvegicus* at the fifth month, showed an increase of 2133% in the experimented animals vs. their corresponding controls. The electrophoretic profile analysis of lipoproteins revealed an increase of 66.5% of VLDL-LDL and a decrease of 92.7% of HDL. However in *Rattus norvegicus*, few variations were shown. The histological examination of the thoracic aorta showed that experimental hypothyroidism induced by the chronic administration of Carbimazole led to structural alterations (intima thickness and media disorder). At the end of our experimentation, the in vitro study of aortic smooth muscle cells (SMC) of hypothyroid animals, revealed an increase in proliferation rate, which reached 135% in *Psammomys obesus* and 68% in *Rattus norvegicus*. These results suggest the implication of hypothyroidism in the development of the atherosclerosis process.

Effects of hyposmotic shock on ATP release in turbot (*Scophthalmus maximus*) hepatocytes. H. Ollivier, K. Pichavant, E. Puill-Stéphan, C. Goanvec, M. Theron, V. Maxime, P. Calves, S. Roy, L. Nonnotte, G. Nonnotte (Unité de Physiologie Comparée et Intégrative, UFR Sciences et Techniques, 6 Av. Le Gorgeu CS 93837, 29238 Brest Cedex 3, France).

Contribution of purinergic signalling to the regulatory volume decrease (RVD) process was examined in isolated hepatocytes of turbot (*Scophthalmus maximus*), a marine flatfish. Hyposmotic stress induces ATP release from cells which stimulates membrane purinergic receptors and triggers cascades of intracellular events. RVD is partially prevented by ATP diphosphohydrolase apyrase and P2 receptor antagonist suramine. Cellular shrink is triggered by ATP added to an isosmotic medium. cAMP potentiates osmosensitive ATP trafficking as adenylyl cyclase activator forskolin increases nucleotide release. By contrast, verapamil, a mdr1 P-glycoprotein inhibitor, and gadolinium, a stretch-activated channels inhibitor, failed to prevent the mechanism, excluding involvement of such proteins in nucleotide export. Hyposmotic swelling of hepatocytes elicits a transient rise in cytosolic calcium concentration ($[Ca^{2+}]i$) which could contribute to ATP release since the calcium ionophore ionomycin caused nucleotide efflux under isosmotic conditions and the calcium chelator EGTA abolished ATP release under hyposmotic conditions. These data provide the first evidence of a volume-sensitive ATP signalling aimed at volume constancy of a marine teleost fish cell type.

Renal alterations induced by injected methionine in rabbit *Oryctolagus cuniculus*. K. Othmani-Mecif, L. Khedis, Y. Benazzoug (Extracellular Matrix, BCM, FSB, USTHB, BP 32, 16111, El Alia Algiers, Algeria).

Methionine, an essential amino acid important in the composition of any diet becomes

a considerable factor of vascular risk when it is introduced in high concentration. The aim of this work consisted in studying the effect of the injection, by sub-cutaneous way, of this amino acid on the uremia and proteinemia and on the histo-morphometry of the rabbit kidney. The experimentation was carried out on local female rabbits which received during one month, 121 mg of methionine.kg^{-1} of body weight per day. The untreated animals received physiological water under the same conditions. The follow-up of uremia showed an elevation at day 15 of treatment followed by a fall at the end; proteinemia increased slowly until the 7th day and then became normal until day 30. The renal histology of treated rabbits showed a thickening of the mesangium, a widening of the blood capillaries and a deposit of conjunctive material between the tubes in the medullary zone. Comparatively to the untreated rabbit, the morphometric study indicates a reduction in the corpuscule axes ($P < 0.05$) with a marked increase in the glomerular room ($P < 0.0001$). The height of the collector and the circumvented distal tubes decreased to a significant degree ($P < 0.01$) whereas the cells of the thin portion of the Henle tube seemed unchanged.

Opening of connexin40, 43 and 45 hemichannels expressed in CHO cells by ATP depletion. I. Plante, D. Fournier, L. Gailis, P. Daleau (Institut de Cardiologie de Québec, Hôpital Laval, 2725 chemin Ste-Foy, Ste-Foy, Canada).

Connexons of adjoining cells dock to form gap junction channels which allow the passage of ions and small molecules. They are composed of six transmembrane protein subunits called connexins (Cx). Cx belong to a multigene family of ~ 20 members. The heart expresses the Cx40, 43 and 45 isoforms. It has been shown that connexons may function as transmembrane ion channels. This study was designed to induce connexon opening by intracellular ATP depletion. cDNA of Cx40, 43 and 45 were individually transfected in CHO cells. We used the patch-clamp technique and a voltage ramp protocol (from –80 to +60 mV in 1.5 s) for measurement of ionic currents. In untreated transfected cells, the normalised slopes of current induced by voltage ramps were minimal (0.04 ± 0.005 nA/V/pF). The presence of 2 mM glucose, 2 mM 2-deoxyglucose and 10 μM antimycin A induced an opening of the connexons. The average slopes for Cx40, Cx43 and 45 and controls (i.e. non-transfected cells) were 1.14 ± 0.58, 1.09 ± 0.35, 0.35 ± 0.06 and 0.08 ± 0.04 respectively (n = 3/group). We also tested the effect of 5 mM 2-deoxyglucose +2 mM glucose on Cx45; the slope was 0.94 ± 0.44 compared to 0.07 ± 0.02 for controls (n = 3/group). Low-ATP induced increase in cell permeability was confirmed using the fura2 fluorescence technique; an accumulation of Ca^{2+} was only observed in the transfected cells. In conclusion, we showed that intracellular ATP depletion is able to induce opening of connexons formed from Cx40, 43 and 45. Thus, opening of hemichannels is likely to develop during cardiac ischemia and to be involved in associated electrical abnormalities.

Excess of methionine induces heart damage. L. Raaf, N. Ben Ahmed, K. Hadj Ziane, M. Rahim, S. Aouichat-Bouguerra, Y. Benazzoug (Laboratoire Matrice Extracellulaire. FSB, USTHB. BP 32 El Alia, Bab Ezzour, Alger, Algéria).

A number of statistic and epidemiologic studies have shown the increase of cardiovascular diseases risk with hyperhomocysteinemic subjects. These suffer from coronary, cerebral, peripheric vessel injuries and thoracic atherosclerosis. As vessels, Hyperhomocysteinemia induces damages in several other organs like the liver, kidney, brain and heart. Our results report alteration of heart histomorphometric properties in experimental hyperhomocysteinemic Wistar rats. Chronic methionine administration at 140 mg.kg^{-1} of weight body/day for 6 months caused collagen, PAS material and cell accumulation in endocardic space. Connective component deposits were furthermore revealed in the myocardium between myocyts but essentially around vessels. This histological data corroborate with morphometric results which indicate thickness of endocarde and vessels wall.

Force-velocity of extensors and flexors trunk muscles under isokinetic conditions. M.

Ripamonti, A. Rahmani, D. Colin (Laboratoire des APS, Université du Maine, Av. Olivier Messiaen, 72085 Le Mans Cedex 9, France).

The aim of this study was to establish a Force-Velocity relationship for the trunk flexor muscles on the one hand, and the trunk extensor muscles on the other hand, under isokinetic conditions. To the authors' knowledge, no study has dealt with this subject. Nine healthy subjects (26 ± 11 years, 75 ± 15 kg, and 176 ± 19 cm) performed a series of flexion and a series of extension on a Biodex dynamometer at 6 various angular velocities 120, 105, 90, 75, 60 and 45.s^{-1} (2.09, 1.83, 1.57, 1.31, 1.05 and 0.78 rad.s^{-1}). The test demonstrated that, to all the subjects, the Force-Velocity relationships obtained were linear for the flexor muscles ($P < 0.01$; $0.85 < r^2 < 0.98$) and polynomial of the second order ($P < 0.03$ and $0.67 < r^2 < 0.98$) for the extensor muscles of the rachis. Several hypotheses are advanced to explain this difference. The main cause seems to be fatigue.

Sensory-specific satiety: could it be diminished by a change in alimentary olfactogustatory stimulation in humans? M. Romer, J. Lehrner, V. Van Wymelbeke, T. Jiang, L. Deecke, L. Brondel (Centre des Sciences du Goût, 15 rue Hugues Picardet, 21000 Dijon, France).

Alimentary sensory pleasure is an important factor in ingestive behavior. Renewal of olfactogustatory pleasure by introducing new foods or through seasoning the previously consumed food might increase intake. To find out whether sensory-specific satiety (SSS) for a food could be modulated, either by introducing a novel food or by a modification of sensory stimulation via minor manipulations upon the food just eaten. One hundred eighty healthy subjects were distributed over 3 experiments involving intake of one out of 6 fresh foods (cucumber, tomato, pineapple, banana, peanut, pistachio). Before and after intake of the olfactorily chosen food, blindfolded subjects rated the foods on the following: Olfactory Pleasure (OP), Specific Appetite (SA) and Stimulus-Induced Salivation (SIS). Exp. 1: one chosen food was repeatedly presented orthonasally and rated before and after it was eaten. Exp. 2: a second food was olfactorily chosen and ingested after the first one. Exp. 3: the same food was offered again after seasoning it. In Exp. 1, 2 min after ingestion, food-intake was limited by SSS and OP, SA, SIS were correlated among each other for eaten and uneaten foods. In Exp. 2, OP for uneaten foods was significantly ($P < 0.01$) increased after ingestion of a chosen food to specific satiety. In Exp. 3, when the food just eaten was seasoned, OP increased ($P < 0.01$) and led to additional intake (80% of the first intake). These results suggest that SSS is not a stable phenomenon, since it was reduced after introduction of a new flavor or after seasoning an ingested food. This could explain how food variety leads to over-consumption.

Oral epithelial cells are involved in innate immunity against fungal (*Candida albicans*) infection through antimicrobial peptides β-defensins. M. Rouabhia, K. Savignac, J. Chakir (Faculté de médicine dentaire, Université Laval, Québec, Canada).

Epithelial cells may be involved in innate immunity against bacterial and yeast infections via a number of broad-spectrum antimicrobial proteins such as human β-defensin-1 (HBD-1) and HBD-2. The aim of this study was to investigate the effect of *C. albicans* on the production of HBD-1 and HBD-2 by oral epithelial cells and to evaluate the effect of these proteins on *C. albicans* growth and morphology. First, oral epithelial cells were infected with 10^5 *C. albicans* for 2, 4, 8, and 24 h. Western Blot testings were performed at the end of each infection time point using proteins extracted from the cells. Second, *C. albicans* was cultured in the presence of HBD-1 or HBD-2 and later seeded on agarose plates. These were incubated for 3 and 6 h and their colonies were assessed. Finally, *C. albicans* was cultured in the presence of HBD-1/HBD-2. Yeast was later added to a medium containing 20% of bovine serum. The morphological changes were followed at 1, 2, 3 and 4 h using an optical microscope. *C. albicans* modulated the production of HBD-1 and HBD-2. HBD-1 and HBD-2 inhibited the growth and morphological changes

of C.albicans. This inhibition was greater when *C. albicans* was in contact with the HBD for a longer period of time (6 h). The important effect was obtained with HBD-2. This study suggests that oral epithelial cells are involved in *C. albicans* growth and morphological changes control via antimicrobial peptides HBD-1 and HBD-2.

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ACE inhibition and endurance exercise capacity in type 1 diabetes mellitus. O. Rouyer, J. Zoll, F. Daussin, P. Helms, F. Thaveau, T. Chataigneau, V. Schini-Kerth, C. Damgé, F. Piquard, B. Geny (Laboratoire de Physiologie et Explorations Fonctionnelles, CHRU, 1 place de l'Hôpital, 67000 Strasbourg, France).

The objective is to determine whether ACEi improves diabetic rat exercise capacity through an improvement in skeletal muscle metabolism and/or endothelial function. Wistar Rats were divided into three groups: control (CTL), diabetics (D), diabetics with perindopril (DP: 6 weeks, 2 $mg.kg^{-1}.day^{-1}$). Type 1 diabetes was induced with intravenous administration of streptozotocin (65 $mg.kg^{-1}$), 8 months before perindopril treatment. After habituation on a treadmill, an exhaustive endurance test (10 $cm.s^{-1}$) was then performed. A week later, endothelial function was determined by thoracic aorta relaxation together with mitochondrial oxidative capacities (V_{max}) in permeabilised fibres of gastrocnemius muscle. D and DP presented enhanced plasma glucose and body weight, compared with CTL. D presented with hypertension (158 ± 12 mmHg) vs. DP (129 ± 4 mmHg) and CTL (130 ± 6 mmHg), $P = 0.02$. Exercise capacity severely decreased in D (28.7 ± 2.1 min) and DP (8.32 ± 1.7 min), compared to CTL (91.5 ± 2.2 min), $P < 0.001$. Similarly, Vmax decreased in D (4.34 ± 0.83 μmol d'$O_2.min^{-1}.g^{-1}$) and DP (4.34 ± 0.85 μmol d'$O_2.min^{-1}.g^{-1}$) vs. CTL (10.32 ± 0.67 μmol d'$O_2.min^{-1}.g^{-1}$), $P < 0.001$. In DP, exercise capacity was correlated with Vmax ($r = 0.79$, $P = 0.033$), with endothelial dependant relaxation being identical in the three groups. In conclusion, skeletal muscle metabolism alterations could partly explain the severe exercise capacity impairment observed in diabetes mellitus rats. The unexpected exercise capacity decrease in the DP group could be related to their blood pressure normalisation and/or diabetes duration.

Results of the "défi" 4S (*Sport-Santé/Sédentarité-Surpoids*) network. G. Scetbon, J. Pouzols, D. Thibaud, G. Connault-Levaï, E. Conte, A. Duvallet, V. Lebar (Centre médico-sportif, Av. Jean Moulin, 77176 Savigny-le-Temple, France).

In September 2003, a health-care network was created in Savigny-le-Temple (Seine-et-Marne) at the initiative of different public organizations: Conseil Général, DDJS, DRDJS, Inspection Académique, Conseil Régional, CDOS and CROSIF. At the center of this network is the "Centre Médico-Sportif" which acts as a link between the medical professionals involved (private doctors, hospital doctors, school medicine practitioners and PMI) and actors of sports activities (clubs and associations). The network is in charge of organizing the medical support and sports activities for overweight children and adolescents. After 18 months of network activity, 78 patients had been followed during more than 400 visits; obesity had been diagnosed by school medicine doctors and nurses for 26% of these patients, by private doctors (general practitioners and pediatricians) for 26% and by the "Centre Médico-Sportif" for 21%. Patients were 6 to 16 years of age at the time of inclusion and the mean age at dectection was 11 years and 5 months. The study population included 62% of girls and 38% of boys. The patients (43%) were initially diagnosed with class 2 obesity, 47% with class 1 obesity and 10% as overweight. During this program of medical and sports activities follow-up, 87 patients participated in one sports activity on an annual basis, 7 patients were also followed in the Melun hospital for paraclinical tests or in case of difficulties in their medical management. Participation in the program was good with only 10 children dropping out of the program, 3 of them because they moved. Considering weight and height development, BMI was reduced or stabilised in 83% of the patients

and augmented in 17%. In our opinion, these results justify the pursuit of this multidisciplinary prevention program.

Effectiveness of counselling overweight and obese patient in the "défi 4S" network (*Sport-Santé/Sédentarité-Surpoids*). G. Scetbon, J. Pouzols, A. Duriez, J.J. Combourieu, V. Lebars, A. Duvallet (Centre médico-sportif, Av. Jean Moulin, 77176 Savigny-le-Temple France).

Obesity is a complex multi-factorial disease with prevalences significantly associated with age, sedentary lifestyle and nutritional education. Prevention during childhood should be considered a priority, since there is a risk of persistence in adulthood. Intervention children showed high scores of efficiency with behaviour modification programmes for healthy eating and physical activity. Management of obesity will require a comprehensive range of effective strategies. The programme was intended to influence physical activity behaviour and dietary behaviour. Physical activity, by increasing energy expenditure had a positive role in reducing fat storage and adjusting balance in overweight patients. The philosophy is aimed at linking all actors of this challenge of a public health problem. The "défi 4S" network was created in 2003 with public organisations (ville de Savigny-le-Temple, Conseil Général de la Seine-et-Marne (77), Conseil Régional d'Île-de-France), government (DRDJS Paris-Île-de-France, DDJS77), general, national education and sports medicine doctors, and clubs or organisations of sports (CDOS77 et CROS Île-de-France). Overweight children were detected by measuring BMI (body mass index). They were classified according to WHO. Identified as "overweight or obesity class I and class II" (BMI < 40), they were addressed to sports medicine practitioners to discuss increasing activities and decreasing of improper eating behaviour. They decided appropriate goals. The patients identified as "obesity classe III" (BMI > 40) were followed by a pediatrician of the Melun general hospital. The first patient was included in November 2003. From this date till now, 135 children have been recruited; all were "less active or inactive". Seventy accepted voluntary to participate (52%). Participation was very good; only 6 patients stopped. They practised 16 kinds of sports, and several for some (basketball 18, swimming and badminton 12, School of sports 10, Athletics 9, dance 5, football 4, table-tennis, cycling and gymnastics 3, handball and judo 2, tennis, karate, boxing and horse-riding 1). The exercise specialists were volunteers having specific training in the "défi 4S" network before they received the first overweight sportsman.

Abnormal SpO_2 in obese adolescents: assessment by functional tests and impact of weight reduction. J.M. Sène, M.L. Frelut, G. Pérès (Physiologie du Sport, CHU Pitié-Salpètrière, AP-HP 75013 Paris, CTP Margency et Hôpital St-Vincent-de-Paul AP-HP 75014 Paris, France).

Aerobic conditions are very important to restore in obese subjects. SpO_2 was measured at rest and during ventilatory tests in obese adolescents (OB) before and after a weight reduction programme (WRP). 11OB (13.7 ± 1.3 y; BMI = 42.3 ± 4.5 $kg.m^{-2}$) were compared to 11 controls (C) (13.8 ± 1.0 y; BMI = 19.1 ± 1.9 $kg.m^{-2}$, $P < 0.0001$) before and after a multidisciplinary WRP (BMI = 32 ± 4.5 $kg.m^{-2}$, $P < 0.0001$) SpO_2 (Nellcor® saturometer) and heart rate (HR, Polar®) were continuously recorded at rest and during an apnea (AT) and a hyperapnea test (HT) of 15 s each. SpO_2 were ≥ 97% in all C and 7/11 OB (normosaturated: Nsat) and < 97% in the 4/11 remaining OB (subsaturated: Ssat). After the WRP, SpO_2 was ≥ 97% in all subjects. The more obese were the adolescents, the lower were their SpO_2. SpO_2 decreased < 94% during AT in 3/11 OB, before but in none after the WRP nor in C subjects. SpO_2 increased in all subjects up to ≥ 98% during the AT, followed by a decrease under the resting value, starting later in Ssat adolescents (102 ± 43 s) than in the Nsat adolescents (51 ± 13 s) and the C group (22 ± 6 s). SaO_2 levels at rest were heterogeneous in OB adolescents, lower than in C adolescents and got worse during an AT. The slower response after SpO_2 variations suggests the existence of significant

differences in the ventilation regulatory mechanisms in OB. In conclusion, the 15 s HT appears to be an appropriate tool in order to detect abnormal ventilatory responses in OB. Our WRP leads to significant SpO_2 improvement and apnea tolerance.

Grant from INSERM.

Antioxidant properties of rosuvastatin were associated with an ischemia-reperfusion cardioprotective effect in normotensive rats. P. Sicard, B. Lauzier, S. Delemasure, C. Vergely, L. Rochette (LPPCE, IFR No. 100, Faculties of Medicine and Pharmacy, 7 Bd Jeanne d'Arc, 21000 Dijon, France).

The aim of this study was to appreciate the consequence of a chronic treatment of normotensive (WKY) and hypertensive (SHR) rats with rosuvastatin on (i) isolated heart function under conditions of ischemia-reperfusion and (ii) oxidative stress reperfusion levels. At 10 weeks of age, SHR and WKY rats were given or not rosuvastatin (per os, 10 $mg.kg^{-1}$ daily for 3 weeks). Systolic blood pressure was assessed every week. Hearts were isolated, perfused (Langendorff) and subjected to 30 min of global ischemia followed by 30 min of reperfusion. Functional parameters (coronary flow, left ventricular developed pressure, heart rate) were measured. Reactive oxygen species (ROS) produced during reperfusion were quantified by electron spin resonance spectroscopy using a spin probe (CP-H, 1 μM). An oxidative fluorescent probe, dihydroethidium was used to localise superoxide anion production in heart slices. In our experimental conditions, 3 weeks of treatment with rosuvastatin did not lower plasma cholesterol levels, but reduced arterial blood pressure in SHR rats (–18 mmHg, $P < 0.01$). Before ischemia and during reperfusion, cardiac functional parameters deteriorated in SHR as compared to WKY hearts. In WKY but not in SHR, rosuvastatin treatment significantly lessened by 50% the post-ischemic contracture enhanced left ventricular developed pressure ($P < 0.05$) and lowered ROS release during reperfusion ($P < 0.05$). Fluorescent quantification of superoxide production in heart slices showed a reduction of coronary arteries staining. In conclusion, chronic treatment with rosuvastatin of normotensive rats enhances myocardial recovery after ischemia-reperfusion and lessens reperfusion-associated free radical production. However, if rosuvastatin can decrease arterial blood pressure in SHR, the myocardial protective effects observed in WKY are no longer present in this hypertensive strain of rats. It is possible that SHR presents a myocardial resistance to the pleiotropic effects of rosuvastatin.

Biventricular stimulation in female patients with chronic heart failure: evaluation of functional parameters after 3 months. J. Siegelová, M. Novák, P. Vank P, J. Jančík, J.C. Eicher, J.E. Wolf, L. Mífková, L. Kožantová, H. Svačinová, P. Dobšák, J. Vítovec (Dept. of Functional Diagnostics and Rehabilitation, St. Anna Faculty Hospital Brno, Faculty of Medicine, Masaryk University, Pekařská 53, 656 91 Brno, Czech Republic).

The objective is this study was aimed at the evaluation of the influence of biventricular stimulation on oxygen uptake and maximal workload in group of female patients with chronic heart failure (CHF) practicing normal activities. A group of female patients ($n = 7$; mean age 69.0 ± 7.2 years) with dilative cardiomyopathy and CHF with implanted biventricular pacemaker (BiV PM) was evaluated. All subjects underwent a spiroergometric test (to symptom-limited maximal level) and 2D echocardiography 14 ± 10 days before BiV PM implantation; the same tests were repeated after 3.0 ± 0.4 months. The following parameters were measured: maximal symptom-limited oxygen uptake ($\dot{V}O_{2SL}$ and $\dot{V}O_{2SL}.kg^{-1}$), symptom-limited maximal workload (W_{SL}) and left-ventricle ejection fraction (LVEF). All the subjects included practiced only standard normal activities. A significant increase of W_{SL} (*64.0 ± 10.2 W vs. 57.0 ± 7.0 W at baseline; $*P < 0.05$) and LVEF (*28.0 ± 5.8% vs. 24.0 ± 3.5% at baseline; $*P < 0.05$) values were observed after 3 months of BiV PM implantation. The statistical analysis of the values of $\dot{V}O_{2SL}$ (1054.0 ± 183.7 $mL.min^{-1}$ vs. 997.0 ± 234.2 $mL.min^{-1}$ at baseline) and of

$\dot{V}O_{2SL}.kg^{-1}$ (16.6 ± 3.05 $mL.min^{-1}.kg^{-1}$ vs. 15.7 ± 2.65 $mL.min^{-1}.kg^{-1}$ at baseline) did not show statistical significance. In conclusion, 3 months of biventricular stimulation improved the functional capacity in female patients with CHF, it was demonstrated by the significant increase of the values of maximal workload and LVEF. Although the evaluation of the maximal oxygen uptake did not show statistical significance, a clear tendency to improvement was present.

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Effects of the playing position and increasing test load on the anaerobic performances in Algerian soccer players. Z. Taoutaou, H. Bounekar, M. Arafa, A. Baz (Laboratoire des APM, INFS/STS de Dely-Ibrahim, BP 71 El-Biar, Alger, Algeria).

The purpose of the study was to compare the anaerobic performances in Algerian soccer players based on the playing position and to assess the effect of increasing test load on anaerobic peak power (Wx; $Wx.kg^{-1}$) and capacity (Wan; $Wan.kg^{-1}$). The study was conducted on 34 soccer players from the national junior team (16 defenders, 8 midfielders, 10 forwards). Their means (± SEM) for age, body mass and height were 18.5 ± 0.96 years; 67.7 ± 1.06 kg; and 175 ± 8 cm, respectively. All subjects performed 30-s cycle sprint (Wingate anaerobic test) against a load of 75 $g.kg^{-1}$ (W75) body weight, vertical jump (H), 10-m (T10) and 50-m (T50) sprints. In addition, 13 soccer players performed the Wingate anaerobic test against two other resistances (90 $g.kg^{-1}$ (W90) and 110 $g.kg^{-1}$ (W110) body weight). The mean values of anaerobic peak power were in defenders: 676.5 ± 33 W (9.55 ± 0.33 $W.kg^{-1}$), midfielders: 575.5 ± 34 W (8.6 ± 0.4 $W.kg^{-1}$), forwards: 645.5 ± 32 W (9.79 ± 0.3 $W.kg^{-1}$). During the Wingate test performed at 75 $g.kg^{-1}$ load, there was no significant difference in anaerobic peak power between players based on positions, although the capacity expressing in relative values was higher in forwards compared to midfielders ($P < 0.05$). The mean values of H, T10 and T50 were similar between groups. There was significant differences between W75 and W90 ((Wx, $P < 0.01$; $Wx.kg^{-1}$, $P < 0.01$); (Wan, $P < 0.01$; $Wan.kg^{-1}$, $P < 0.01$)); W90 and W110 (Wx, $P < 0.01$; $Wx.kg^{-1}$, $P < 0.01$) and between W75 and W110 (Wan, $P < 0.01$; $Wan.kg^{-1}$, $P < 0.01$). It was concluded that the peak power measured during the Wingate test, vertical jump, 10-m and 50-m performances were not affected by the playing position.

The non toxicity of mineral elements after oral administration in the rat. L. Tekaya-El Manoubi, E. Fehri, A. Ayadi, P. Galle (Laboratoire de Physiologie, Faculté de Médecine de Tunis, 15 rue Jebel Lakhdhar, 1007 Bab Saâdoun, Tunis, Tunisia).

The chemical toxicity of several mineral elements after parenteral administration is well known. Among these elements are Indium and especially Aluminium whose frequent intoxication is linked to its presence in dialysis water when used for patients treated for chronic kidney failure. Its accumulation in the neurone lysosomes is responsible for the occurrence of encephalopathies and its accumulation in the bone for the occurrence of bone demineralisation and spontaneous fractures. The aim of this work was to show the behaviour of the intestinal mucosa, liver and kidney after a simultaneous oral administration of both aluminium and indium. Two methods of observation and microanalysis were used: the conventional transmission electron microscopy and the secondary ion mass spectrometry. The results showed that aluminium and indium were selectively concentrated in the same lysosomes of duodenum enterocytes as no soluble phosphate form, so there was no specialised lysosome for a given element. These precipites were later eliminated with apoptotic cells in the intestinal lumen in less than 72 h. The efficiency of this phenomenon is shown here because of the absence of these elements in the liver and kidney. It is suggested that the duodenum could play an important role because of the limitation of toxic element diffusion in the plasma.

N-3 fatty acids-deficient rats exhibit impaired acquisition of an olfactory discrimination task. S. Ullah, M. Rialland, F. Datiche, F. Liénard, A. Hichami, J.M. Chardigny, M. Cattarelli, N.A. Khan (UPRES Lipides et Nutrition, Université de Bourgogne, 6 Bd Gabriel, Dijon, France).

Diets enriched with n-3 polyunsaturated fatty acids (PUFA) n-3 exert beneficial effects in health and disease. In order to elucidate the role of dietary n-3 PUFA in olfactory discrimination, the rats were fed, for two generations, on a diet which induced in vivo deficiency in n-3 PUFA contents. The experiments were performed on n-3 PUFA-deficient diet (PUFA-DD)-fed rats of the second generation (F2). The control rats were fed a balanced diet (BD). The rats fed PUFA-DD and BD were submitted to an olfactory discrimination task learning in a four-arm maze where they had to associate one odour of a pair with a water-reward. The PUFA-DD fed rats showed a slower acquisition of the olfactory discrimination task compared to the BD fed rats. At the end of the conditioning, all the rats were sacrificed and the analysis of fatty acid composition in different brain areas (olfactory bulb, hippocampus, cortex piriform and neocortex) was performed. Feeding PUFA-DD to rats resulted in a loss of around 80% of DHA in total lipids and phospholipids in different brain areas. The decrease in DHA contents in PUFA-DD rats is correlated with an increase of docosapentaenoic acid (22:5 n-6) levels in all the brain areas of these animals. We also studied the expression of phosphorylated proteins (Fos, Egr1, CREB, MAP Kinase) which are involved in cell signalling. We observed that the expression of these phosphorylated proteins was not highly significantly different in BD and PUFA-DD rats. At present, we are investigating the expression of several genes, involved in synaptic transmission, in different brain areas of these animals.

Autonomic function assessed by heart rate variability in frail elderly people with postural abnormalities and in control subjects. V. Van Wymelbeke, F. Mourey, D. Moreau, M. Buchheit, P. Pfitzenmeyer, L. Brondel (Centre Européen des Sciences du Goût, 15 rue Hugues Picardet, 21000 Dijon, France).

Heart rate variability (HRV), which is considered to reflect the activity of the autonomic nervous system (ANS), has been reported to decline with age. The aim of the study was to explore autonomic nervous activities in older patients showing Psychomotor Disadaptation Syndrome (PDS) through 24-h ECG recordings.The study included a PDS group (14 patients, 84.5 ± 6.9 years) and a control group (13 frail subjects without postural abnormalities, 80.6 ± 6.7 years). ANS was assessed using the standard deviation of the all normal R-R intervals (SDNN), the square root of the mean squared differences of successive R-R intervals (RMSSD), the percentage of interval differences of successive R-R intervals greater than 50 ms (pNN50), then for spectral analysis using total power (Ptot) and power density in the low-frequency (LF) and high-frequency (HF) bands. SDNN of the PDS group was lower than that of the control group both for the day and the night periods ($P < 0.05$) and RMSSD was lower both for the 24 h and the night periods ($P < 0.05$). Total power (Ln Ptot) was lower in the PDS group than in the control group for the 24 h, day and night periods ($P < 0.05$). Values of Ln LF and Ln HF were also smaller for the PDS group than for the control group for the 24 h, day and night periods ($P < 0.05$). The decrease of ANS activity observed in PDS subjects was then more important that the alteration found in normal ageing.

Modulation of antioxidant status in alcohol-related diabetes mellitus in Beninese subjects. A. Yessoufou, K. Moutairou, A. Girard, M. Fatoké, J. Prost, H. Ahissou, F. Djrolo, G. Avodé, D. Amoussou-Guenou, A. Hichami, N.A. Khan (Université de Bourgogne, Département de Physiologie, UPRES Lipides et Nutrition, Dijon, France).

In the present study, we investigated the antioxidant status in diabetes mellitus, related or not to alcohol consumption. A total of 38 type 1, 48 type 2 and 42 alcohol-related diabetes patients were selected by specialist clinicians

from an Insulin Bank (Diabetic Centre) and Endocrinology Department of the Centre National Hospitalier et Universitaire of Cotonou, Benin (West Africa). Total antioxidant status was assessed through the oxygen radical absorbance capacity of the plasma and the determination of enzymatic and non-enzymatic antioxidant molecules. Serum triglycerides, total cholesterol and HDL-cholesterol concentrations were determined and the lipid peroxydation was evaluated by specifically measuring thiobarbituric acid reactive substances (TBARS) assay. Plasma total antioxidant capacity was more decreased in alcohol-related diabetes patients than in type 1 and type 2 diabetes patients, regardless of the complications (retinopathy and renal failure). Plasma vitamin E concentrations were significantly decreased whereas those of vitamin C increased in all diabetic patients compared to the controls, irrespective of the complications. In addition, superoxide dismutase and glutathione peroxidase activities were reduced in all patients (type 1, type 2 and alcohol-related), irrespective of the complications. Glutathione reductase activity was diminished in type 1 and alcoholic, but not in type 2, diabetic patients. Excessive alcohol consumption appears as an oxidative aggravating factor in diabetes mellitus. Besides, alcohol-related diabetes highly resembles type 1 diabetes as far as the antioxidant parameters are concerned.