Abstracts congresos internacionales 2008

(Por disposición del Comité Editorial de la Revista, solo se publicarán *abstracts de* congresos internacionales, europeos y americanos).

DENTOMAXILOFACIAL

19TH CONGRESS OF THE IADH (INTERNATIONAL ASSOCIATION FOR DISABILITY AND ORAL HEALTH), SANTOS, BRASIL.

BUCAL STATUS IN DISABLED CHILDREN. HOSPITAL DE NIÑOS ROBERTO DEL RÍO.

Rojas C, Araneda L, Pinto M, Weber N.

Introduction. Children with special needs are those whose dental care is complicated by a physical, mental, or social disability. They have tended to receive less oral health care, or of lower quality, than healthy children. And also around 55% of families of disabled children live in poverty. It has been studied that children with disabling conditions had a considerably higher dmft index than children without disabling conditions. The proportion of children with caries experience was higher also. Objectives. To demonstrate that the bucco dental state of disabled children is different from a group of healthy children. Sample and methods. 36 children of the Hospital de Niños Roberto del Río, with different disabling conditions were examinated and compared with 58 healthy children A clinical data template was built based on WHO criteria, including dental records, like type of dentition, caries indexes, hygienic and gingival indicators and enamel characteristics. Results. The study and control group did not showed statistic differences between them for DMFT – dmft indexes, oral debris, plaque index and enamel defects. There was a significative differences for gingival index and the number of deciduous teeth with untreated caries that need to be extracted, these values were higher for the study group compares with the controls. Conclusions. Children with disabling conditions have higher prevalence of gingival inflammation and oral damage for deciduous teeth with untreated caries that need to be extracted compared to healthy children.

DERMATOLOGÍA

88TH ANNUAL MEETING OF THE BRITISH SOCIETY OF DERMATOLOGISTS, LIVERPOOL, INGLATERRA.

BODY SITE DISTRIBUTION OF SQUAMOUS CELL CARCINOMA IN CHILE. ANALYSIS IN TWO SOCIOECONOMIC STRATA.

V. Zemelman, CY Valenzuela, V Tomulic, G Zamalloa, J Roa.

Squamous cell carcinoma (SCC) has increased in Chile in the past decade. UVB radiation is an important factor in the pathogenesis of SCC. Previous studies on skin colour in the Chilean population showed that individuals from the low stratum (35-40% Amerindian) were darker than those from the high stratum (0-20% Amerindian). The purpose of this research was to study and compare the site distribution of SCC in these two different socioeconomic strata in Chile. For this, a total of 2041

SCC tumours was analysed; 1459 tumours from five state hospital were compared with 582 tumours from private clinics. Statistical analysis was performed by chi-square and z for proportion tests. Women and men from the low socioeconomic strata showed a significantly higher number of SCC in the face and in the genital area. On the other hand, men from the higher strata showed a significantly higher number on the scalp and upper extremities; females from high stratum showed a higher number in upper and lower extremities. On the other hand, in the SCC body distribution by gender, men from both strata showed a significantly higher number of SCC in scalp and ears than females. Furthermore, females from both strata showed a higher number of SCC on the cheeks and on the lower extremities. The different distribution in both strata may be explained by genetics factors, different pattern of sun exposure and cultural differences. Also, the different site distribution of SCC in men and women may be explained by a different sun exposure pattern in both sexes, scalp and ears are more sun exposed in males than females.

17TH CONGRESS OF EUROPEAN ACADEMY OF DERMATOLOGY AND VENEROLOGY, PARIS, FRANCIA

OMEGA – 3 FATTYACIDS PROTECT ATOPIC PATIENTS AGAINST ULTRAVIOLET INDUCED ERYTHEMA

M.Gaete, J.F.Honeyman

Background: Dietary n-3 fatty acids have an anti-inflammatory activity, decreasing PGE2 production. PGE2 is an inflammatory prostaglandin that polarizes immune response to Th2. On the other hand atopic dermatitis is a chronic inflammatory Th2 mediated skin disease. Up to date few studies of n-3 fatty acids supplementation to atopic patients have been reported and no one has evaluated the cutaneous anti-inflammatory response. Objective: The aim of this study in atopic patients was to determine the effect of an oral n-3 fatty acids supplementation on minimal erythema dose. Methods: Thirty six patients with atopic dermatitis were included in a randomized study. Eighteen patients were supplemented with 600 mg of n-3 fatty acids daily, and eighteen patients received placebo during 2 weeks. Minimal erythema dose (MED) and SCORAD index were determined before and after the intervention. Results: After two weeks, n-3 supplemented group showed significant reduction in cutaneous inflammatory response. N-3 supplementation increased MED from 52,4 ± 10,9 mj/cm2 to 65,3 ± 15,9 mj/cm2 (p 0,001) . It was associated with a decrease in subjective symptoms. Conclusion: In atopic patients oral administration of n-3 fatty acids increased minimal dose erythema showing a cutaneous anti-inflammatory effect. Our results highlight the importance of n-3 dietary supplementation in atopic dermatitis.

CARATENOIDS COMBINED WITH VITAMIN A AND E PROTECT AGAINST UV-INDUCED ERYTHEMA

J. F. Honeyman, A. M. Cabezas, M. Gaete

Background: Ultraviolet radiation exposure is associated with photo-aging and skin carcinogenesis. Erythema induced by UV is partially mediated by oxidative damage. Antioxidants have been recently considered as a therapeutic option for preventing photo-damage. Carotenoids, vitamin C and vitamin E are well known as antioxidants due to their role in scavenging reactive oxygen species. Objective: To assess the protective effects of oral supplementation of a balanced mixture of carotenoids, vitamins C and E, against UVB induced erythema. Methods: Thirty females (36±10 years; mean±SD) with phototype III were enrolled into the study. An oral supplement (Imedeen Tan Optimizer®) containing lycopene (3,8 mg), palm fruit extract (19,5 mg, approx 30% natural mixed carotenoids) plus vitamin C (60 mg) and vitamin E (10 mg) was administered daily, during a 4-month period. Minimal Erythema Dose (MED) was determined at baseline (57,6 ± 23,1mJ/cm2), after one, two and four months of oral administration and also at two months after ending supplementation. Results: MED increased significantly after administration of the oral supplement at two and four months of administration, 21,6% ($p<0,05$) and 39,6% ($p<0,01$), respectively. MED returned to baseline value at two months after ceasing oral supplementation. Conclusion: This study demonstrates that oral intake of a relatively low dose, but balanced mixture, of natural carotenoids (including lycopene), vitamin C and E, provides an increasing cumulative protection against UV induced erythema. Systemic photo-protection contributes to a permanent UV defense and should be considered as a strategy against the adverse effects of ultraviolet radiation.

THE ENDOCRINE SOCIETY'S 90TH ANNUAL MEETING, SAN FRANCISCO, USA.

EFFECT OF EXERCISE ON CIRCULATING BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) IN OVERWEIGHT AND OBESE SUBJECTS.

AV Araya, X Orellana, J Pino, D Godoy, J Espinoza and L Soto.

In animal models exercise can increase BDNF expression, neuroplasticity and neuroprotection. On the other hand, BDNF can regulate appetite and caloric intake. Objectives: To evaluate in overweight and obese subjects the effect of aerobic exercise on levels of circulating BDNF. To evaluate spontaneous caloric intake before and after the training period. Methodology: 15 subjects, 7 males and 8 females, BMI 27 kg/m2, age between 26-51 yr were included. Diabetes, depressive or psychiatric disorders, coronary disease, locomotor dysfunction and BMI over 35 kg/m2 were exclusion criteria. In all of them, percentage of fat mass and muscular arm area were calculated with the Durnin and Womersley equation. A self reported record was used to calculate daily caloric intake before and after 3 month of a training program of aerobic exercise. Plasma, serum and platelet BDNF were measured in basal condition and at the end of month 3. Subjects were advised to continue their usual caloric intake. Results:

Clinical and biochemical characteristics before and after 3 month of aerobic exercise training

	Basal	After 3 month	p
n	7M/8F		
Age (years)	38.3 ± 9		
BMI (kg/m2)	30.6 ± 2.3	30.1 ± 2.4	0.01
Waist (cm)	108.1 ± 5.8	105.1 ± 6	0.003
% fat	35.2 ± 6.6	33.3 ± 6.8	0.0029
Muscular arm area	5157.3 ± 1098.6	5475.8 ± 1453.6	0.06
Syst BP (mmHg)	128.7 ± 14.6	122.6 ± 13.3	0.05
Diast BP (mmHg)	82.3 ± 10.1	72.6 ± 7.7	0.007
Daily Caloric intake (cal)	2142.3 ± 593.6	1805 ± 507.6	0.01
Serum BDNF (ng/ml)	2.4 ± 1.7	7.8 ± 5.5	0.001
Plasma BDNF (ng/ml)	0.9 ± 0.4	2.2 ± 3.3	0.06
Platelet BDNF (pg/platelet 106)	6.2 ± 5.4	23.3 ± 20.5	0.005

$p<0.05$ was considered statistical signifficant.

The table shown a significant decrease in BMI, waist circumference, percentage of fat and diastolic blood pressure. Also, a spontaneous decrease in caloric intake was observed. At the end of the training period, we observed a significant increase in serum BDNF and platelet BDNF. Final plasma BDNF correlated positively with the percentage of weight lost ($r=0.78$, $p=0.0005$) and final platelet BDNF correlated directly with the reduction in caloric intake. Conclusions: aerobic exercise can increase serum and platelet BDNF in overweight and obese subjects. The reduction in the caloric intake could be related with the effect of BDNF in appetite regulation.

20TH INTERNACIONAL CONGRESS OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE (IFCC-WORLDLAB 2008), FORTALEZA, BRASIL

A NOVEL PROGNOSTIC MARKER IN OVARIAN CANCER.

Muñoz M, Geraldo MO, Gabler F, Tapia V, Moyano L, Owen G, Selman A, Vega M, Romero C.

Introduction: each year, more women die from ovarian than from any other gynecologic malignancy. The lifetime risk of diagnosis with ovarian cancer is 1,7% and the annual incidence approaches 61,3 per 100,000 in women 75 to 79 years of age. Ovarian cancer is highly vascularized and aggressive, with VEGF being a principal factor responsible for angiogenesis, vascular permeability and metastasis. VEGF is secreted by various tumours and is involved in tumour progression and

maintenance. During recent years, it has been demostrated that nerve growth factor (NGF) through activation of its high affinity receptor (trkA) promotes angiogenesis in many tissues and induces VEGF expression in ovarian cancer. Objetives: to evaluate trkA protein expression in epithelial and endotheliai cells from ovarian tissues through the progression of the ovarian cancer to ascertain if trkA receptor in epithelial ovarian cancer may be considered as a prognostic marker. Material and methods: 42 samples of ovarian tissue (seven samples of: inactive normal ovary, benign, borderline ovarian tumours and serous epithelial ovarian cancer: EOC, GI, EOC GII, EOC GIII; seven samples for each type of tissue) were obtained from the departments of Obstetrics and Gynecology and Pathology within the Faculty of Medicine at the Universidad de Chile, within full Ethical Committee approval. All specimens were fixed in 10% buffered formalin. Formalin-fixed ovarian tissues were cut in 6-µm sections, where trkA and NGF were evaluated by immunohistochemistry (IHC). NGF, trkA and trkA-p expression levels in epithelial cells (ovarian surface epithelial cells and inclusion cyst epithelial cells from inactive normal ovaries and transformed epithelial cells from ovarian tumours and carcinomas). The trkA expression in endothelial cells from ovarian tissues was also evaluated by IHC. Furthermore, we evaluated the effect of NGF secreted by ovarian cancer explants on the vasculogenesis in vitro, using the trkA receptor expressing endothelial cell line EAhy962. The IHC evaluation was determined as the percentage of positive stained cells. In all cases, trkA protein in epithelial and endothelial cells from ovarian tissues was evaluated by three independent observers and blinded to patient category and the positive staining was assessed in at least 1000 cells per sample. The evaluation of trkA expression in endothelial cell was compared with the diameter of blood vessels per area of tissue (µm2). ANOVA test was used to ascertain significance between groups. Results: epithelial cell trkA receptor and NGF expression show a significant increased in ovarian carcinomas compared with inactive normal ovaries $p<0.001$ (table). The activated receptor (trkA-p) is expressed only in moderately and poorly differentiated ovarian carcinomas. The trkA receptor endothelial cell expression also increased in poorly differentiated ovarian carcinomas (EOC III) and these results correlate to the diameter of blood vessels per tissue area. Finally, NGF secreated from cultured EOC increased angiogenic potential in our in vitro model. Conclusions: these data suggest that NGF may be a direct angiogenic factor in ovarian tissue and that the immunodetection of trkA receptor may be a novel prognostic marker in ovarian carcinomas.

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carcinomas compared with inactive normal ovaries p<0.001 (table). The activated receptor (trkA-p) is expressed only in moderately and poorly differentiated ovarian carcinomas. The trkA receptor endothelial cell expression also increased in poorly differentiated ovarian carcinomas (EOC III) and these results correlate to the diameter of blood vessels per tissue area. Finally, NGF secreated from cultured EOC increased antigenic potential in our in vitro model. Conclusions: these data suggest that NGF may be a direct angiogenic factor in ovarian tissue and that the immunodetection of trkA receptor may be a novel prognostic marker in ovarian carcinomas.

EXPRESSION OF MOLECULAR MARKERS IN THYROID CARCINOMA AND THEIR ASSOCIATION WITH NODAL MATASTASES.
Tapia V, Fernández C, Cabané P, Gac P, Lanas A, Pineda P.
BACKGROUND. Papillary carcinoma of the thyroid is the most common malignant tumor of the thyroid gland, accounting for 80% of all thyroid cancers in the US. Overall, it accounts for 1% of all cancers. These tumors may arise at any age but are most common between the 3-5th decades and twice as common in women. These tumors usually have a good prognosis but may invade the lymphatic leading to metastases to the regional lymph nodes and occasional spread beyond the neck in 5-75% of cases. In Chile studies at national level do not exist but diverse groups have shown an increase in the incidence of this neoplasia, which has been attributed to diverse factors not yet characterized. The prognosis of this carcinoma is generally favorable, with an accumulated mortality from 5 to 6 by billion inhabitants. Diverse systems of classification have been elaborated and allow establishing prognosis (survival and recurrence risk). Nevertheless, cases of tumors initially considered of low risk by size or histological variant can have great aggressiveness, with invasion of neighboring tissues and metastasis. Invasion and metastasis is a process of multiple stages that implies invasion of the tumor capsule, spread to the surrounding tissues and penetration to blood and lymphatic vessels. In literature a great number of macromolecules that take part in proliferation, invasion and angiogenesis have been described that could explain this behavior. Among them, NIS (sodium iodide symporter), is a transmembrane protein mediating the active transport of iodide in the thyroid gland, fundamental step in the synthesis of thyroid hormones. Its expression has been studied in normal thyroid and a reduced expression in thyroid tumor cells has been observed. The c-MET also known as hepatocyte growth factor receptor (HGFR), is a membrane receptor that is essential for embryonic development and would healing and it had been found to be deregulated in many types of human malignancies. MET is normally expressed by cells of epithelial origin, while expression of HGF (hepatocyte growth factor), the only known ligand of the MET receptor is restricted to cells of mesenchymal origin. Upon HGF stimulation, MET induces angiogeneis and metastasis. Previous studies by inmunohistochemistry have shown contradictory results since MET expression has been described upregulated but also downregulated in the thyroid cancer. TIMP1 (tissue inhibitor of metalloproteinases 1) is a endogenous inhibitor of the matrix matalloproteinases (MMPs), a group of peptidases involved in degradation of the extracellular matrix. In addition to its inhibitory role against most of the known MMPs, the encoded protein is able to promote cell proliferation in a wide range of cell types, and a may also have an antiapoptotic function. TIMP1 is over expressed in diverse neoplasias and recently it has been detected in thyroid carcinoma. EphrinB2 is transmembrane protein-tyrosine kinases and has been implicated in mediating developmental events, especially in the nervous system and in erythropoiesis. Recently it has been detected over expressed in numerous tumors and would be involved in angiogenesis processes. Our hypothesis is that the level of expression of molecular markers in papillary cancer (NIS, c-MET, TIMP1 and EphrinB2) can have a significant association with histological aggressiveness and thus can be used for prognoses in the postoperative management of these patients. The aim of the study is to detect the presence of markers previously associated to the papillary cancer and to correlate their level of expression with criteria of histological aggressiveness and initial prognosis. METHODS. Papillary carcinoma from 12 patients was analyzed in this study. There were 7 patients with papillary carcinoma without evidence of metastatic lymph node and 5 papillary carcinoma with metastatic lymph nodes. Specimens were procured under protocol approved by the Institutional Ethical Committee. Immunohistochemistry was used to examine paraffin-embedded tissue sections derived from both group for the expression of NIS, c-Met, EphrinB2 and TIMP1. RESULTS. Immunostaining of paraffin-embedded tissue sections with an antibody against NIS revealed marked specific immunoreactivity confined to cytoplasmatic compartment in sections derived from the two studied groups (papillary carcinoma with and without metastasis). We did not find any differences in the levels of this staining after compare both groups. In the case of c-MET, we found that had a strong expression associated to both nuclear and cytoplasmic compartments but we did not find differences in the levels of this staining after compare both groups. The EphrinB2 expression was mainly cytoplasmic in both group, nevertheless after evaluated the nuclear immunoreactivy, we found a statistical significant decrease (p<0.05)

in metastatic samples group. Finally, TIMP1 immunoreactivity appeared to be decrease in the metastatic group, although this difference was not significant, which is consistent with results shown in literature. CONCLUSIONS. Our preliminary results suggest that the translocation from nuclear to cytoplasmic compartment may be an initial step to get enough EphrinB2 to initiate and perhaps maintain the angiogenesis process required in metastasis. In the same way a decrease expression in TIMP1contributes to matrix degradation and facilitates tumor cell invasion and metastasis.

WOMEN WITH POLYCYSTIC OVARIAN SYNDROME AND INSULIN RESISTANCE SHOW A DISMINUTION IN THEIR ENDOMETRIAL INSULIN SIGNALING PATHWAY.

Rosas C, Fornes R, Vantman D, Romero C, Vega M.

Background. The Polycystic Ovarian Syndrome (PCOS) affects 4 – 12% of women in fertile age. This pathology is characterized by irregular menstrual cycles, anovulation and androgen excess. The high circulating levels of androgens disturb the function of several tissues of the organism, including the endometrium, which exhibits alterations in the expression and function of several molecules, as we have previously reported. In addition, 50-70% of the patients with PCOS present insulin resistance, suggesting a deregulation of the insulin signaling pathway in different tissues. As Known, insulin activates the mechanisms involved in the expression of glucose transporters (GLUT4) located at the plasma membrane level; besides, in the endometrium insulin action would assure the energy substrate for processes such as tissue homeostasis and uterine receptivity. The insulin-receptor complex stimulates the activity of PI3kinase (PI3K) and subsequently, Akt/PKB which phosphorylates several substrates, among them the AS160 protein with GTPase activity. The protein AS160 represents one of the most important regulators of GLUT4 translocatoion to the cell surface in response to insulin action, which has multiple phosphorylation sites, being threonine in the position 642 (Threo642) essential for the translocation of GLUT4. With the inactivation by phosphorylation of AS160-GTPase activity, some Rab proteins associated to vesicles with GLUT4 are activated and the vesicular traffic with GLUT4 to the plasma membrane is enhanced. Therefore, the phosphorylation level of AS160, especially in Threo642, is crucial for the presence of GLUT4 in the cell surface, which could permit glucose availability for the fulfillment of fertility-related processes in the endometrium. On the other hand, insulin receptors exposed in the plasma membrane could be related to ligand concentration in the extracellular media and also, the relationship between insulin receptor and AS160, are indispensable for signal transduction that controls the expression of GLUT4 at the plasma membrane level. Objectives. To evaluate whether the function of AS160 is altered in endometria obtained from PCOS women with and without insulin resistance compared to controls. Also, to determine if the endocrinologic and metabolic status of these women affect the expression of insulin receptors. Methods. Endometrial samples were obtained with a Pipelle suction curette from women with PCOS, as assessed by the Rotterdam Consensus criteria, attending the Infertility Unit of the University of Chile Clinical Hospital; the control endometrial samples were obtained from fertile healthy women at the time of bilateral tubal ligation or hysterectomy for benign uterine disease at the University Hospital. Oral glucose tolerance test (OGTT) was performed to all patients with PCOS in order to evaluate insulin resistance. The endometrial specimens were classified as endometrium obtained from control women (n=8); from PCOS patients without insulin resistance (n=8) or endometrium from PCOS women with insulin resistance (n=8). Blood levels of insulin, testosterone and Sex Hormone Binding Globulin (SHBG) were determined and those patients with insulin levels higher than 60 µIU/mL after OGTT, were classified as having insulin resistance. Endometrial protein levels of insulin receptor, AS160, AS160 phosphorylated in Threo642, were assessed by Western blot. This investigation was approved by the University of Chile Clinical Hospital and School of Medicine Ethical Committees, and informed written consent was obtained from all subjets. Results. Blood levels of testosterone, SHBG and the free androgen index (FAI) were similar in the groups of patients studied, independent of their insulin resistance condition. Nevertheless, a marked difference in the levels of basal insulin between both groups of PCOS patients was obtained, being approximately 50% higher in PCOS patients with insulin resistance. The analysis by Western blot showed that the protein levels of insulin receptor and of AS160 were similar between the groups; although, AS160 phosphorylated in Threo642 was significantly lower in endometria from patients with PCOS and insulin resistance, compared with those tissues obtained from control and PCOS patients with normal levels of insulin ($p<0.05$). The correlation and linear regression studies indicated that in endometria from PCOS women with insulin resistance, an inverse relationship between basal insulin levels and protein insulin receptor and AS160, were found ($p<0.05$). On the other hand, a positive association was obtained between the protein levels of insulin receptor and AS160 in tissues obtained from PCOS women; nevertheless, this relationship diminished in PCOS women with insulin resistence ($p<0.05$). Conclusions. The data of the present investigation show that in the endometria

from patients with PCOS and insulin resistance, AS160 exhibits a lower function, without being affected its protein levels. At the same time, the loss of the relation between insulin receptor protein levels and AS160 in these endometria, could be a consequence of a decreased protein levels of these receptors in response to the high levels of basal insulin found in these patients. Supported by FONDECYT # 1050098.

MEDICINA NUCLEAR Y PSIQUIATRÍA

50TH ASH ANNUAL MEETING AND EXPOSITION (AMERICAN SOCIETY OF HEMATOLOGY), SAN FRANCISCO, USA.

EVIDENCE OF ENDOTHELIAL DYSFUNCTION IN COCAINE USERS.

Jaime Pereira, Claudia G. Sáez, Julio Pallavicini, Paulina Olivares, Olga Panes, Natalia Moreno, Sabine Belmont1, Teresa Massardo and Diego Mezzano.

Background: Cocaine abuse is associated with an increased risk of cardiac and cerebrovascular events, such as myocardial infarction, sudden cardiac death, and ischemic stroke. The underlying mechanisms leading to these complications are not fully understood although intravascular thrombus formation and accelerated atherosclerosis are prominent findings. In this sense, in vitro studies have demonstrated that cocaine may induce damage and/or activation of endothelial cells. The structural and functional integrity of the endothelium is essential for the maintenance of vascular homeostasis and its damage plays a critical role in the pathogenesis of vascular disease. Endothelial dysfunction may be assessed by testing the impaired vasodilator response to a stimulus or by measuring the release of plasma markers of endothelial damage. Increased number of circulating endothelial cells (CECs) has been reported in several pathologic conditions associated with severe vascular damage and its enumeration in peripheral blood is currently considered a reliable method to assess endothelial damage. We hypothesized that chronic exposure to cocaine induces endothelial damage which could be expressed by increased CEC counts in peripheral blood. Methods: Twenty cocaine-dependent subjects (aged 19-52 years, mean age 30 years) and 25 healthy, matched controls (aged 20-49 years, mean age 31 years) were studied; all patients fulfilled DSM-IV criteria for cocaine dependence with drug exposure within the 72 hours prior to blood sampling. CECs were isolated from peripheral blood by use of immunomagnetic beads coated with anti-CD146, stained for CD45 and Ulex Europaeus lectin 1 and counted under fluorescence microscopy. MCP-1, sICAM-1, von Willebrand factor and high-sensitivity C-reactive protein (hsCRP) were measured by enzyme-linked immunosorbent assay. Results: Compared to controls, CECs were significantly elevated among cocaine users (632 ± 281 vs 67 ± 54 cells/mL, $p<0.0001$). Plasma levels of sICAM-1 (360±92 ng/mL) and MCP-1 (166±71 pg/mL) were increased in cocaine-dependent individuals compared to the controls (261±34 and 67±29, respectively; $p< 0.01$). The hsCRP levels were significantly increased (6.8 mg/L); however plasma von Willebrand factor concentration was not different between patients and controls (86.4±22 vs 70.5±16%, respectively; NS). Levels of CECs correlated positively with sICAM-1 (r: 0.7; p: 0.003) and hsCRP (r: 0.56; p: 0.0037). Conclusions: Highly increased number of CECs and significant increments in soluble plasma markers of endothelial perturbation were found in cocaine dependent individuals. This is the first demonstration of endothelial dysfunction among these individuals and our findings support the notion that cocaine-induced endothelial damage may play a pathogenic role in the ischemic vascular disease observed in chronic cocaine users.

55TH ANNUAL MEETING AMERICAN SOCIETY NUCLEAR MEDICINE (SNM), NUEVA ORLEANS, USA.

BRAIN PERFUSION DEFECTS ARE ASSOCIATED WITH HEMOSTATIC SYSTEM ACTIVATION IN CHRONIC COCAINE USERS.

Teresa Massardo, Julio Pallavicini, Juan Carlos Quintana, Rodrigo Jaimovich, Olga Panes, Patricia Hidalgo, Diego Mezzano and Jaime Pereira.

Objectives: Cocaine consumption induces cortical brain perfusion defects, but their pathophysiology is not completely understood. Vasospasm plays a role and cocaine may activate the hemostatic system. Our goal was to examine the association between hemostasis activation and brain perfusion, in patients with recent cocaine consumption and under strict abstinence. Methods: We studied 10 cocaine dependent men (24-49 y.o.) according to DSM-IV criteria, with confirmed recent use of cocaine. Basal brain perfusion SPECT was performed and hemostasis activation assessment: P-selectin, phosphatidilserine (PS) and CD40L expression on platelets; tissue factor (TF) on circulating monocytes and circulating plasma microparticles

(n°, cellular origin and procoagulant activity [PCA]) by flow cytometry, platelet PCA and thrombin antithrombin complex [TAT]). Results: In 10/10 perfusion baseline abnormalities were significantly correlated with platelet P-selectin (r:0.69;p<0.02) and PCA in microparticles (r:0.88;p=0.007). When cut-off point was set for brain perfusion defects severity, TAT, microparticles, PS, P-Selectin and TF were significantly increased in patients with more severe parenchymal damage (75th percentile). Control SPECT performed a month later in 8/10 patients during abstinence, showed multiple small bilateral reversible foci. Conclusions: Cocaine use activates the hemostatic system and appears to be related to severity of cortical perfusion abnormalities. Confirmation of these findings on a larger number of patients is warranted.

NEUROLOGÍA

INTERNATIONAL CONGRESS OF MYOLOGY 2008, MARSELLA, FRANCE.

DYSFERLINOPATHY IN CHILE, THE TWO FIRST CASES REPORTED SHOW TWO NOVEL MUTATIONS.

Bevilacqua JA; Krahn M; Pedraza L; Gejman R; Gonzalez S; Lévy N.

Dysferlinopathies are autosomal recessive muscular dystrophies caused by mutations in the dysferlin (DYSF) gene that encodes for dysferlin (MIM 603009). Dysferlinopathy manifests as two main clinical phenotypes, distal Miyoshi's myopathy and LGMD2B, however a wide range of clinical phenotypes --- ranging from sub-clinical to severe forms may also be produced by similar mutations We are reporting the two first Chilean cases of dysferlinopathy with a molecular genetic analysis. A 26 year old man, from a consanguineous marriage, developed distal myopathy involving the posterior compartment of both legs. Impairment progressed in the in the lapse of three years to tights and the anterior compartment the right arm. CK levels at onset were 21237 UI/dl. Biopsy of the quadriceps showed unspecific dystrophic changes, and absent dysferlin immunostaining. In this patient, a novel one base-pair deletion of the exon 21 was identified (c.1948delC) at a homozygous state. This leads to a shift of the reading-frame resulting in a premature termination codon (p.Leu650TyrfsX6). The second case is a 26 year old woman that developed a progressive weakness in her right leg. Examination showed an asymmetrical atrophy of the calves and both anterior recti. Normal walking was impaired, but other muscular groups were less affected. CK levels at onset were 8870 UI/dl. Biopsy of the quadriceps showed minimal dystrophic changes, dysferlin immunostaining was absent. Two disease-causing mutations, at a compound heterozygous state, were detected in her: a frame shifting mutation of the exon 27 (c.2858dupT, p.Phe954ValfsX2) and a novel missense mutation of the exon 13 (c.1276G>A, p.Gly426Arg). The latter, was not retrieved in 200 control chromosomes and affects a highly conserved amino-acid residue located in C2 domain C of dysferlin. We conclude that this novel missense change is pathogenic Further studies to typify dysferlinopathy in the region will contribute of this dystrophy.

DYNAMIN 2 MUTATIONS IN AUTOSOMAL DOMINANT CENTRONUCLEAR MYOPATHY.

Bitoun M; Prudhon B; Durieux AC; Bevilacqua JA; Romero NB; Guicheney P.

The autosomal dominant centronuclear myopathy (CNM) is a rare congenital myopathy characterized by delayed motor milestones, facial and muscular weakness often associated with bilateral ptosis. The typical muscle histopathology comprises central nuclei, predominance and hypotrophy of type 1 fibres, and radial arrangement of sarcoplasmic strands. Phenotypic variability has been observed ranging from mild forms, with slowly progressive myopathy occurring during adolescence or later, to more severe neonatal presentation. Since the identification of the first mutations in the DNM2 gene encoding the dynamin 2 (DNM2), sequencing of this gene led us to identify 13 heterozygous mutations in 39 CNM families covering the entire clinical spectrum. Four out of the 13 mutations cause severe neonatal CNM and are located in the ?-helix of the Pleckstrin Homology domain which is involved in targeting proteins to the plasma membrane. The severity of the phenotype associated with these mutations suggests that this region is particularly important for DNM2 function in muscle. DNM2 is a large GTPase involved in endocytosis, Mitogen-Activated Protein Kinase (MAPK) pathway activation, actin assembly and is a component of the centrosome, the main microtubule organizing center. We constructed vectors allowing in vitro and in vivo expression of GFP-tagged proteins. DNM2-mutants are able to impair the clathrin-mediated endocytosis and the EGF-induced ERK1/2 MAPK activation in transfected COS7 cells. Among these mutants, the p.R465W was expressed in the mouse tibialis

anterior muscle by electrotransfer, showing a mislocalization compared to wild-type DNM2. Additionally, immunocytochemical analysis of muscle biopsies from DNM2-CNM patients demonstrate that the localisation of some proteins involved in nuclear positioning is modified. Our results suggest that the association in the muscle fibres of structural alterations and MAPK pathway impairment could be important in the pathophysiological processes of the DNM2-related CNM.

"DARK NECKLACE" FIBERS MYOPATHY A PECULIAR MORPHOLOGICAL PATTERN OF CONGENITAL MYOPATHY.
Bevilacqua J, Bitoun M, Oldfors A, Stoltenburg , Claeys K, Maugenre S, Prudhon B, Lacène E, Brochier G, Manéré L, Ferreiro A, Lafôret P, Eymard B, Biancalana V, Guicheney P, Fardeau M, Romero N.
Congenital myopathies are characterized by peculiar structural changes of muscular fibers. Recently, working on a series of cases close by their clinical and pathological features from the centronuclear myopathies, we identified a group of patients which presented a curious morphological pattern characterized by the presence of a variable amount of "dark necklace" fibers (DNF). Necklace fibers were found in both type1 and type2 fibers. They showed a basophilic subsarcolemmal ring deposit, few micrometers apart from the plasma membrane. The ring stained intensively with HE, GT, NADH-TR, SDH and COX, but was not detected on the myofibrillar ATPase. Occasional nuclei align with the necklace. EM analysis showed that the necklace was situated about 3µm from the sarcolemma. It consists of normally oriented and disorganized myofibrils with remarkably small diameter, surrounded by increased, normally structured mitochondria and numerous sarcotubular profiles. Immunohistochemical studies showed an intense labeling using anti-SERCA1 and SERCA2 antibodies, but not with other proteins of the sarcoplasmic reticulum (calsequestrin, ryanodine receptor, triadin), and the T-tubule (dihydropyridine receptor-alpha1subunit). In addition, there was a marked reaction with anti-desmin and aB-crystallin antibodies, but not for myotilin antibodies. Clinically, the four cases identified were sporadic. Symptoms began in the first decade, as a slowly progressive proximal pattern of weakness predominantly in lower limbs. No facial or extraocular muscle involvement was observed. Serum CK were slightly elevated in two cases and normal in the two others. Electromyography showed unspecific myopathic changes in all of them, in one case nerve conduction studies showed distal slowing of latencies. The peculiar structural alterations were not present in any other cases of centronuclear myopathies. Preliminary molecular genetics analysis allowed to exclude DNM2 and BIN genes. MTM gene study is in progress. The mechanism of this structural defect in myofibrillar organization and organelle positioning remains to be elucidated.

MORPHOLOGICAL REAPPRAISAL OF CENTRONUCLEAR MYOPATHY (CNM) AFTER THE IDENTIFICATION OF DNM2 MUTATIONS.
Bevilacqua J, Bitoun M, Taratuto A, Monnier N, Guicheney P, Fardeau M, Romero N.
Muscular biopsies of congenital myopathy patients showing a high rate of central nuclei as the most important finding were usually classified as having CNM. With the identification of DNM2 mutations as the cause of autosomal centronuclear myopathy (Bitoun et al. 2005), two main groups arose from CNM patients, those mutated on DNM2 and those excluded for DNM2 mutations (about 50% of patients in each group). Interestingly, myotubular myopathy and some recessive forms of CNM myopathy are caused by mutations in proteins functionally linked to DNM2 (i.e. myotubularin, amphyphisin-2). We reviewed a large series of biopsies with diagnosis of CNM before DNM2 mutation identification. According to our observations, proper observation of morphological criteria is important to orientate molecular analysis of the different CNM subgroups. Nuclear "centralization" is very typical of DNM2 related cases, and should be distinguished from random nuclear "internalization". Additional structural alterations within muscular fibers are another criterion useful to suggest or discard DNM2 related CNM. Typical aspects of radiating sarcoplasmic strands "spoke of wheel" pattern is seen with mutations in DNM2 almost exclusively. On the other hand, the association of nuclear internalization (but no centralization) with pseudo-core lesions would lead to mutations in RYR1 as the first possibility. Amongst the CNM diagnosed cases, we identified at least two other subgroups. One showing internalized nuclei associated with a peculiar subsarcolemmal alteration that resembled a "dark lace". In these cases, nuclei aligned with the "lace" of distorted material. In another group, nuclear internalization was higher than normal but the hallmark of the biopsy was the presence of rounded fibers with a strong subsarcolemmal positive staining with oxidative techniques. Percentages of fibers with centralized or internalized nuclei, with associated histopathological features (i.e. presence or not of radiating sarcoplasmic strands) are good indicators for underlying genotypes.

MYOPATHY AND AXONAL CHARCOT-MARIE-TOOTH DISEASE.
Bitoun M, Prudhon B, Durieux Ac, Bevilacqua J, Stojkovic T, Oldfors A, Maurage Ca, Eymard B, Fardeau M, Romero N, Guicheney P.
Dynamin 2 (DNM2) mutations have been associated with two distinct clinical presentations: autosomal dominant centronuclear myopathy (CNM), a congenital myopathy, and dominant intermediate and axonal Charcot-Marie-Tooth disease (CMT), a peripheral neuropathy. To date, the sequencing of DNM2 gene has lead us to identify 13 heterozygous mutations in 39 CNM families and one mutation in an axonal CMT patient. Five DNM2-CNM mutations are located in the middle domain (MD), seven in the Pleckstrin Homology (PH) domain and one in the GTPase effector domain (GED) of the protein. The CMT-DNM2 mutation (p.K559del) is located in the PH domain in which five DNM2 mutations have been previously identified. Therefore, mutations in the PH domain cause both CNM and CMT. PH domains are classically involved in targeting proteins to the plasma membrane. Structural studies of this domain from other proteins suggest that the ı-sheets in the N-terminal part of the domain are involved in the interaction with membrane phosphoinositides and that the C-terminal part includes an ı-helix involved in protein-protein interactions. Four out of the seven CNM-mutations in this domain, affecting residues 618, 619 and 625 in the ı-helix, cause severe neonatal CNM. The 6 CMT-DNM2 mutations are restricted to a region from position 537 to 570 that includes the ı-sheet region. Only one CNMDNM2 mutation (p.E560K) was located in this 'CMT region' and is associated with an atypical presentation of CNM. This CNM mutation p.E560K is associated with the muscle morphological features of CNM, which are absent in the CMT patient with the p.K559del mutation. These data enlarge the spectrum of DNM2 mutations in CNM and CMT and highlight the clinical and morphological heterogeneity associated with DNM2 mutations. The severity of the clinical phenotype associated with ı-helix PH domain CNM mutations suggests that this region is particularly important for DNM2 function in muscle.

PSIQUIATRÍA

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CHILEAN VALIDATION STUDY OF MDQ.
Paul Vohringer.
Introduction: This study tested the validity of the Mood Disorder Questionnaire's (MDQ) Spanish version, a screening instrument for bipolar I and II disorders, in adult outpatients of the Mood Disorders Clinic (MDC) at the Instituto Psiquiátrico de Santiago de Chile. Methods: A total of 202 patients attending the aforementioned outpatient clinic were screened with the MDQ between April 2006 and November 2007. A research professional, blind to the MDQ results conducted a diagnostic interview using the bipolar module of the Structured Clinical Interview for DSM-IV (SCID I). Results: A Mood Disorder Questionnaire screening score of 7 or more items yielded good sensitivity (0.66) and a very good specificity (0.82). The translated MDQ was found internally consistent (alpha Cronbach 0.73). The instrument showed a high concurrent validity with the SCID I. Conclusion: The Mood Disorder Questionnaire is a useful screening instrument for the bipolar disorder patients in the Chilean population.

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SEROTONIN TRANSPORTER PROMOTER POLYMORPHISM AND NEUROTICISM IN CHILEAN BORDERLINE PERSONALITY DISORDER PATIENTS INSTITUTIONS
Juana Villarroel, Maria Leonor Bustamante, Natalia Roa, Cristian Montes, Wilson Vielma, Aldo Solari, Patricia Iturra, Sonia Jerez, Hernan Silva.I
Objective: to investigate the relationship between 5-HTTLPR polymorphism and personality traits in Chilean patients with borderline personality disorders. Methods: we studied 52 subjects (37 woman and 15 man) who met the DS M-IV diagnostic criteria for borderline personality disorder according to the International Personality Disorders Examination, without axis I diagnoses and drug-free at the moment of evaluation. Personality traits were assessed with the Spanish version of Eysenck Personality Questionnaire Revised (EP Q-R). 5-HTTLPR polymorphism, and TPH 1, 5HT 1B, 5HT 2C receptors polymorphism were genotyped by PCR from peripheral blood. Results: S-allele carriers (LS and SS genotype) showed higher scores in Neuroticism dimensions ($P<0.01$) than LL allele genotype patients. The differences were independent from gender and age. In the total sample, women were significantly more

neurotic than men (P<0,01), but this difference appears only in the S-carriers patients. Meanwhile the LL genotype patients scores lower in Neuroticism than S-carriers and without differences between men and women. No significant association was observed between 5-HTTLPR polymorphism and other EPQ-R personality dimensions. No significant association was observed between personality dimensions and the other studied polymorphism. Conclusion: S-allele carriers have higher scores in Neuroticism dimensions in the Chilean patients with borderline personality disorder studied. (Proyecto FONDE CYT N 1071045).

WORKING MEMORY DEFINES TWO BORDERLINE PERSONALITY DISORDER SUBPOPULATIONS.
M. Leonor Bustamante, Juana Villarroel, Matías Ríos, Valeria Francesetti, Patricia Iturra, Aldo Solari, Sonia Jerez, Hernán Silva.
Al M: Working memory refers to transient representation of task-relevant information, and it is crucial for the development of complex, goaloriented behavior. It has been found to be impaired in some psychiatric disorders and to be associated with the functional outcome of patients. In Borderline Personality Disorder (BPD), a severe mental disorder, previous studies suggest that memory systems may be affected, but a specific neuropsychological profile has not been established. The purpose of this work was to evaluate the performance of a group of BPD patients in a working memory task and to compare it to that of a group of individuals without psychopathology. METHODS: We evaluated a sample of 85 individuals, 51 patients with BPD and 34 controls, using the Tower of London (Drexel UniversityVersion) task and analyzed the data using latent class cluster analysis. The clinical evaluation included the IPDE interview to diagnose BPD, a semistructured psychiatric interview to exclude Axis I pathology, as well as structured impulsivity and aggression measures. RESULTS: The model that best fitted the data was a three class model. One class was formed exclusively by controls, while BPD belonged to two different classes. 79% of the patients had a performance on the task that was indistinguishable from that of controls, while 21% of the patients performed significantly worse on the task. CON CLUSIONS: This study suggests that neuropsychologically BPD is heterogeneous. This work was supported by Project Fondecyt 1030305.

REUMATOLOGÍA

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COMPARISON OF THE CLINICAL EFFICACY OF TWO DIFFERENT IMMUNOSUPPRESSIVE REGIMENS IN PATIENTS WITH CHRONIC VOGT-KOYANAGI-HARADA DISEASE (VKH).
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Purpose: Many rheumatic diseases have been associated with uveitis, and thus rheumatologists are frequently consulted in the diagnosis and management of patients with uveitis. The purpose of this study was to prospectively compare in an open randomized trail, the efficacy and safety of two immunosupresive regimens on the clinical outcome in patients with active VKH in spite of systemic glucocorticoid treatment. Methods: Forty two patients with VKH syndrome were diagnosed between 1998 and 2005 in Los Andes Ophthalmologic Foundation, Santiago, Chile (a tertiary national center for diagnosis and management of ocular inflammatory diseases). Twenty one patients developed chronic intraocular inflammation in spite of glucocorticoid treatment and were randomized to receive either prednisone and azathioprine (AZA) (n=12) or prednisone and Cyclosporine (CyA) (n=9). Treatment regimens and their respective outcomes (visual acuity, and inflammation score) were compared. Visual acuity was converted to LogMAR for analysis. Results: Patients from both groups presented an overall good clinical response. In AZA group Tyndall score decreased from 1.21 ± 1.10 to 0.29 ± 0.62 ($p < 0.01$), and visual acuity improved from 0.32 ± 0.35 to 0.096 ± 0.161 ($p< 0.001$). In CyA group Tyndall score decreased from 1.67 ± 1.08 to 0.16 ± 0.51 ($p < 0.001$), and visual acuity improved from 0.41 ± 0.40 to 0.25 ± 0.42 ($p< 0.001$). No differences were found between groups for most of the outcomes, except for the average prednisone dose until remission was achieved. Patients from AZA group had a significantly higher average prednisone dose (23.89 ± 9.49 mg/day, 717.77 ± 284.34 mg/month and total cumulative dose 2705.56 ± 1602.84 mg) than patients from CyA group (14.86 ± 8.89 mg/day and 445.71 ± 266 ± 61 mg/month and total cumulative dose 1275 ± 577.96 mg), $p< 0.01$ for each comparison. Conclusions: Both treatment regimens showed a good clinical efficacy in patients with chronic VKH, however CyA seems to be a better glucocorticoid sparing agent than AZA. M.