Polymorphisms in the gene that encodes the glucocorticoid receptor (GR), an essential regulator of the hypothalamic-pituitary-adrenal axis, have been linked to some psychiatric disorders. Considering that psychiatric manifestations are present in nearly all patients with hypercortisolism, we hypothesized a possible correlation of polymorphisms in the GR gene and clinical and psychiatric manifestations, in CD. To investigate the frequency and clinical implications of the GR gene polymorphism Bcl-1 in patients with CD, we conducted a cross-sectional, case-controlled study. Fifty-three Brazilian patients with CD aged between 12 and 75 years and one hundred healthy controls aged between 42 and 67 years, of both genders, who provided written informed consent, were enrolled. Blood samples were collected from patients for DNA extraction and sequencing for analysis of the GR gene polymorphism Bcl-1. Clinical data (obesity, skin lesions, muscle weakness, hypertension, diabetes, hypokalemia, and sex-related disorders) were obtained through retrospective analysis of medical records, appointment with endocrinologist and with psychiatrist. Mini International Neuropsychiatric Interview, scales self-applicable of anxiety and depression were used to address psychiatric conditions. From the 53 patients studied, 48 were women (90,56%), and 16 patients had macroadenoma (2 of them had tumors larger than 4 cm). Overall frequencies of the Minor Allele for Bcl-1 polymorphism, which corresponds to the risk allele for psychiatric illness in the normal population, did not significantly differ between CD patients (67.92%) and controls (74.00%). Similarly, differences in Minor Allele Frequencies among subgroups of patients presenting with psychiatric and clinical manifestations of CD were not statistically significant. Although data from the literature strongly suggests a correlation between Bcl-1 polymorphism with psychiatric disorders (especially depression) in the normal population, this association was not observed in our cohort of patients with CD. More studies are needed to better clarify a possible role for GR gene polymorphisms as modifiers of the spectrum of psychiatric and clinical manifestations of CD.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Estrogen Synergistically Interacts with Optic Atrophy Protein 1 to Promote Thrombosis

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SUN-572

Thrombosis is a major concern in: premenopausal females on oral contraceptives, menopausal women undergoing hormone replacement therapy, postmenopausal women and transgender individuals receiving estrogen supplementation. The mechanisms linking estrogen exposure with increased thrombosis risk is incompletely understood. Analysis of platelet transcripts in the Framingham cohort identified Optic atrophy 1 (OPA1) expression as being highly predictive of female sex and correlating with increased risk of diabetes and cardiovascular disease. OPA1 regulates mitochondrial fusion, electron transport chain (ETC), complex assembly, cristae morphology and apoptosis. Thus, to determine the functional relationship between platelet OPA1 expression and platelet function in relation to sex steroids we generated mice with platelet specific deletion of OPA-1 protein (pOPA1KO). Male pOPA1KO exhibited structurally and functionally compromised mitochondria with a 50% reduction in mitochondrial DNA and respiration. Male pOPA1KO mice exhibited a prothrombotic phenotype they had: increased agonist-induced activation, shortened time to stable occlusion of the carotid artery as assessed *in vivo* by (rose Bengal) photochemical injury (~25 min knockout vs ~ 35 min control), and were more prone to develop a thrombus (14/15 knockouts vs. 4/8 controls) following permanent ligation of the inferior vena cava. In contrast, female pOPA1KO mice had normal mitochondrial structure, function and DNA. Both agonist-induced platelet activation and thrombus formation was unchanged in pOPA1KO females. Paradoxically, pOPA-1 KO female mice had increased time to stable occlusion of the carotid artery as assessed by photochemical injury (~75 min Knockout vs ~35 min control). Notably, when platelets from pOPA-1 KO or control males were transferred into females following depletion of endogenous platelets, the reconstituted male platelets acquired the phenotype of female pOPA-1 KO mice. Thus, the time to stable occlusion of the carotid artery following photochemical injury was increased. Similarly, reconstitution of male mice with female pOPA1KO platelets were no longer prothrombotic. Gonadectomized pOPA1KO males had an increased time to stable occlusion and gonadectomized female pOPA1KO no longer exhibited increased time to stable carotid artery occlusion. Eugonadal pOPA1KO male mice treated with estrogen exhibited the pOPA1KO female thrombotic phenotype, with increased time to stable occlusion relative to control males. Additionally, OPA-1 levels were positively correlated with increased platelet aggregation and increased estrogen levels in third trimester pregnant human females. Together, these findings reveal a synergistic interaction between platelet OPA1 levels and estrogen to promote thrombosis.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Comparative Histopathology of Endocrine Glands in Phthalate Exposed Male Wistar Rats Unveil the Vulnerability of Adrenal Gland and Augmented by Molecular Docking

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SAT-710

Limited research has been conducted on adrenal gland as a target of endocrine-disrupting chemicals (EDCs). Moreover,

studies on steroidogenesis as the target of EDCs has also attracted lesser attention compared to other metabolic pathways. We studied the effects of two extensively used phthalate esters viz., di-ethyl hexyl phthalate (DEHP) and di-butyl phthalate (DBP) on the adrenal gland in Wistar rats and checked its susceptibility against the exposure of these extensively used phthalates categorized as EDCs. Male rats were divided into seven groups (n = 6). Group I (control) received only corn oil (as a vehicle). Group II, III and IV were treated daily with DEHP at the dose of 250, 750 and 1500 mg/kg-BW respectively *per os* for 14 days. Group V, VI and VII were treated with a daily dose of DBP 100, 500 and 1000 mg/kg-BW respectively *per os* for 14 days. The comparative histological observation of endocrine glands i.e., pituitary, pineal, thyroid, parathyroid, adrenal gland and testes unveil that changes in adrenal gland towards the DEHP and DBP were more remarkable compared to other endocrine glands. Glucocorticoid biosynthesis pathway in the adrenal gland was analyzed by molecular docking of DEHP and DBP with the enzyme proteins involved in the pathway using Maestro Schrodinger 9.4 software. It showed the potential of DEHP and DBP to inhibit these proteins comparable to the known inhibitors of enzymes involved. The present study used a novel approach of *in silico* and *in vivo* to elucidate the sensitivity of adrenal gland towards EDCs through the analysis of the sensitivity of adrenal steroidogenesis on exposure to two widely distributed phthalates with environmental and human health risk potential.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Primary Aldosteronism in Intracerebral Hemorrhage. Not Intracerebral Hemorrhage in Primary Aldosteronism.

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SAT-544

Background: Patients with primary aldosteronism (PA) are more prone to cardiovascular complications including intracerebral hemorrhage (ICH) than those with essential hypertension. But how about PA in ICH patients - not ICH in PA patients? Since ICH patients with PA are at high risk for recurrent hemorrhage and other complications, diagnosis of PA is important even after the occurrence of ICH. Here we aimed to clarify the clinical features of PA in ICH patients at the largest scale ever and to evaluate the efficacy of PA screening with machine learning.

Methods: Out of 181 ICH patients admitted to our hospital between June 2016 and February 2017, 126 patients of hypertensive ICH were enrolled in this study. Plasma aldosterone concentration (PAC), plasma renin activity (PRA) and other hormones were measured in the morning two days after admission.

Results: After leaving out those who had been taking medications which could intervene with PAC or PRA on admission, nine patients were positive for PA screening (PAC/PRA ratio >200 and PAC >120 pg/mL) and 53 were negative. Age (68.6 vs 68.5 y), sex (male 66.7 vs 69.8 %) and blood pressure (172/97 vs 177/100 mmHg) were similar between these two groups. Bleeding volume (14.6 vs 16.2 mL) was also similar, but the lesion was more common in thalamus rather than putamen in PA positive group. Serum potassium was slightly lower in positive group (3.6 vs 3.9 mmol/L; P=0.096) on admission, and the difference became more evident two days later (3.7 vs 4.0 mmol/L; P=0.040). There were no differences in other hormones including cortisol and catecholamine. As for prognosis, PA positive patients had more severe motor or cognitive impairments. Dimension reduction procedure using t-SNE certainly divided these patients into clusters compatible with PA screening tests. Further, we extrapolated this result to 21 patients who had been taking medications which could lower PAC/PRA ratio such as ACE inhibitors, ARB or diuretics and were excluded from the analysis above. K-nearest neighbor method revealed that even in those who had been taking PAC/PRA lowering medications, PAC/PRA ratio >160 could be regarded as positive for PA screening.

Discussion: This is the largest study ever that investigated the clinical features of PA in ICH patients. Contrary to expectations, ICH patients with PA were not necessarily younger than those with essential hypertension. But they were more likely to have severe outcomes even though blood pressure and bleeding volume were similar. This may be partly because of higher aldosterone. The difference in serum potassium was masked on admission probably due to increased sympathetic activity. But about two days later, when its activity peaked out, lower serum potassium in PA positive group became more evident. This can support the efficacy of PA screening tests even in ICH patients, so PA screening should not be awaited just because they have developed ICH.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Analytical Performance and Clinical Value of AMH Testing

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SAT-016

The clinical uses for of anti-Mullerian hormone (AMH) measurements have risen dramatically over the past 5 years. This increase has been driven by the release of fully automated immunoassay systems with European and FDA approval of AMH measurements for assessing ovarian reserve in women presenting at fertility clinics. Most recently the MenoCheck® AMH method was cleared by FDA as an aid in determining menopausal status in women