the corticotropin test. Seventy-three (41%, CI95%: 34-48%) patients had an insufficient response to the corticotropin test. Neither the risk of adrenal insufficiency, unstimulated nor stimulated P-cortisol levels were directly associated with any of the GR SNPs. However, for both insensitive SNPs 9β and ER23/23EK the effect of current prednisolone dose on stimulated P-cortisol was smaller (higher dose did not suppress the cortisol level as much) in carriers vs. non-carriers (p=0.035 and p=0.0075). The same sensitivity-associated tendency was seen for the N363S, but not the *Bcl*1 SNP. The *Bcl*1 SNP occurred more frequently in our cohort compared with control groups (63% vs. 40%, p<0.0001). The same trend was seen for the other sensitive but less frequent SNP N363S. The 9β SNP also occurred more frequently in our cohort (18% vs. 13%, p=0.029), but depending on regional sub cohorts in one control group.
CONCLUSION: The GR SNPs did not directly associate to the risk of adrenal insufficiency, unstimulated nor stimulated cortisol levels, respectively. However, the effect of prednisolone dose on stimulated cortisol depended on the GR SNPs: Cortisol was less suppressed with higher current prednisolone dose in patients carrying the insensitive SNPs. The substantially higher frequency of the *Bcl*1 SNP is remarkable even with modest n=239. It questions whether there is an association between carrying the sensitive GR SNPs and inability to taper GC treatment ending up in this cohort of long-term treated patients.

Pediatric Endocrinology

PEDIATRIC OBESITY, THYROID, AND CANCER

Risk of Long-Term Endocrine Sequelae in Survivors of Progressing Childhood Optic Pathway Glioma Treated by Upfront Chemotherapy: Preliminary Analyses of 102 Subjects from the French Multicentric BB-SFOP Registry

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MON-098

For the brain tumor committee of SFCE (Societe´ Française des Cancers de l'Enfant). Objective: Therapeutic approach favors chemotherapy as the first-line-treatment in progressing OPG. There are few data on long term endocrine outcomes of aggressive OPG treated by upfront chemotherapy. Our main objective was to describe the long-term endocrine sequelae in these patients and to identify potential early predictors of the endocrine involvement. Subjects and methods: Children diagnosed with OPG at an age younger than 16 years from the French multicentric BBSFOP registry were included. They were treated with upfront chemotherapy according to the BB-SFOP protocol in France between June 1990 and December 2004, and subsequent treatment (second-line chemotherapy, surgery, radiotherapy) was used depending on tumor progression. They underwent a late evaluation with clinical and biological assessment between January 2011 and March 2016. Results: One hundred and two patients were included in our study. The mean age at tumor diagnosis was 3.3±0.3 years. The mean time of follow-up was 13.9±3.7 years. A history of precocious puberty was present in 36% of the subjects. At least one endocrine deficiency was present in 93% of the subjects (GHD 74%, TSH deficiency 57%, ACTH deficiency 36%, hypogonadotropism 33%, gonadic deficiency 30%, diabetes insipidus 15%; inappropriate AVP secretion 7%). 37% of males and 39% of females were overweight or obese. Mean adult height, reached in 51 subjects, was -1.2±1.3 SDS in males, and -0.7±1.4 SDS in females. Chemotherapy only was protective from pituitary deficiencies (odds ratio 0.19 to 0.37, $P < 0.05$). NF1 was protective from TSH and ACTH deficiencies (odds ratio 0.25 to 0.35, $P < 0.05$). Tumor volume on diagnostic MRI was not predictive of pituitary deficiencies. Gonadic deficiency was significantly more frequent in males than females (46,5% vs 12.2%, $P < 0.05$), and associated with chemotherapy only (OR 3.2, $P < 0.05$) and NF1 (OR 4.8, $P < 0.05$). Overweight/Obesity was associated with ACTH deficiency (OR 5, $P < 0.05$).Conclusion: Obesity and late endocrine dysfunction were frequent in subjects treated by upfront chemotherapy for aggressive OPG during childhood. However, chemotherapy only, when possible, was protective from pituitary involvement.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Systematic Screening Reveals Large Number of Undiagnosed and Untreated Cardiovascular Risk Factors in Adults with Prader-Willi Syndrome

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MON-284

Introduction: Prader-Willi syndrome (PWS) is a complex hypothalamic disorder, combining hypotonia, intellectual disability (ID), pituitary hormone deficiencies and hyperphagia. In PWS, up to 3% of patients die every year. In half of the patients, the cause of death is obesity related and / or of cardiovascular (CV) origin.
Obesity is caused by hyperphagia combined with a low energy expenditure. Untreated hormone deficiencies like hypogonadism and hypothyroidism can cause low muscle mass and low basal rest metabolism (BRM) leading to this low energy expenditure. Patients with PWS should exercise one hour daily to compensate for their low BRM. However, hormone deficiencies usually cause fatigue, leading to exercise intolerance. Musculoskeletal and / or behavioral problems can also cause reduced physical activity. The subsequent sedentary lifestyle can induce CV risk factors like hypertension, hypercholesterolemia and diabetes mellitus (DM).
Another risk factor often present in PWS is sleep apnea, which can be central (CSA), obstructive (OSA) or both. Both CSA and OSA can lead to pulmonary hypertension and a further increase in obesity.
The above mentioned health problems often remain unnoticed and untreated, which is partly due to the behavioral phenotype of PWS (patients seldomly report pain and hardly ever complain about physical problems). However, if left untreated, these risk factors can cause CV complications leading to hospital admission or even death. To reveal yet

undiagnosed health problems, we performed a systematic health screening among adults with PWS.
Methods: We systematically screened 115 adults with PWS (mean age 31.4 ± 12.1 y, mean BMI 31.8 ± 9,5 kg/m^2) for the presence of undiagnosed health problems and cardiovascular risk factors. Based on a medical questionnaire, medical file search, extensive interview, thorough physical examination and biochemical measurements we made an overview of the undiagnosed health problems in adults with PWS. If possible, we performed polygraphy to test for sleep apnea.
Results: Undiagnosed health problems (hypertension, DM, hypercholesterolemia, sleep apnea, hypothyroidism and hypogonadism) were present in 50% of the patients. 10% had multiple undiagnosed health problems simultaneously. All males and 94% of females had hypogonadism and 15% had hypothyroidism. Hypertension and / or hypercholesterolemia were present in 20% and DM was present in 16%. One third of patients was not on a diet and 22% exercised less than 30 minutes a day. Sleep apnea was present in 17 of 26 patients tested.
Conclusion: We detected a striking number of undiagnosed health problems among adults with PWS which, if left untreated, can pose a serious health threat. Systematic screening is needed to detect these problems in an early phase. This will prevent burdensome and expensive complications and might even reduce mortality in this vulnerable patient population.

Reproductive Endocrinology

OVARIAN FUNCTION — FROM OLIGOMENORRHEA TO AMENORRHEA

Single-Cell Profiling of Adult Human Ovarian Cortex Reveals Six Main Cell Types but No Germline Stem Cells

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OR31-03
The human ovary orchestrates sex hormone production and undergoes monthly structural changes to release mature oocytes. The outer lining of the ovary (cortex) has a key role in defining fertility in women as it harbors the ovarian reserve. It has been suggested that oogonial stem cells exist in the ovarian cortex and that these can be captured by DDX4 antibody isolation. Our study aimed at comprehensive characterization of all cell types present in the ovarian cortex, including the previously reported oogonial stem cells. We developed methods to dissociate human ovarian cortex to a viable single cell solution allowing subsequent analysis by single cell transcriptomic profiling and cell surface antigen screening. In all analyses, cells captured by DDX4 antibodies (DDX4 Ab+) were included as a reference. High quality ovarian cortex tissue from gender reassignement and caesarean section patients was used in the analyses. Our single cell transcriptomic analyses based on >24,000 cells revealed the presence of six main cell types in ovarian cortex; oocytes, granulosa cells, immune cells, endothelial cells, perivascular cells, and stromal cells. Surface marker screening showed robust expression of 43 cell surface antigens in ovarian cortex cells. With the help of transcriptomic and cell surface antigen profiles, the DDX4 Ab+ cells were identified as perivascular cells. This finding was validated by immunostaining of ovarian tissue showing DDX4 Ab+ cells lining CD31 positive endothelial cells of blood vessels. To search for germline stem cells on a broader front, we compared our data with human fetal ovary cells including pre-meiotic germ cells (Li et al. 2017) and found no evidence for the presence of germ line stem cells of any kind in adult human ovarian cortex. In summary, we provide the first cell map of human ovarian cortex. Our results demonstrate six main cell types, but cannot provide support to the existence of oogonial stem cells. This dataset will be a valuable tool for studying the role of specific cell populations in ovarian biology, dissecting causes of infertility, and developing novel assisted reproductive technologies or even contraceptives.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

ACTH-Derived Peptide Antagonists as an Alternative Treatment Strategy for Congenital Adrenal Hyperplasia

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MON-185
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by different enzyme deficiencies in the steroid hormone synthesis leading to a disturbed cortisol biosynthesis. The medical treatment of CAH includes suboptimal ACTH-suppressing high glucocorticoid doses to reduce adrenal hyperplasia and overproduction of androgens. These inappropriate corticoid substitutions are often associated with undesirable side effects such as arterial hypertension, growth failure and obesity. Since the current therapy of patients with CAH is often unsatisfactory, innovative treatment options are required.
The aim of our study was to specifically block the melanocortin 2 receptor (MC2R) signaling pathway as an alternative treatment strategy for CAH. We tested ACTH-derived selective peptides with incorporation of various synthetic non-natural amino acids in the activation motif of ACTH. To study the antagonistic activity of the peptides, cAMP production of MC2R/MRAP stably transfected human embryonic kidney (HEK) 293 cells were measured. All new synthesized peptide antagonists reduced ACTH-stimulated MC2R activity as competitive inhibitors indicated by a reduced *in vitro* cAMP response. Cells pre-incubated with peptide LNP009 showed the most