(5.1 vs 3.2 days, P=0.000), increased total hospital charges ($51,904 vs $34,471, P=0.002), increased odds of cerebrovascular accident (0.8% vs 0.1%, AOR: 5.01, 95% CI 1.1-22.2, P<0.034) and increased odds of acute respiratory failure(4.4% vs 1.3%, AOR: 3.01, 95% CI 1.8-5.0, P<0.000) compared to those without AF.

Conclusions: Patients admitted primarily for hyperthyroidism with co-existing AF had similar inpatient mortality but with longer LOS, increased total hospital charges, increased likelihood of having cerebrovascular accident and acute respiratory failure when compared to those without AF.

Thyroid
THYROID HORMONE METABOLISM AND ACTION

Chronic Stress During Adolescence Blunts the Exercise-Induced Expression of Thyroid Hormone-Target Genes in Metabolically Active Tissues of Male and Female Rats

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Voluntary exercise activates HPT axis[1], that contributes to energy mobilization and energy expenditure. Chronic stress in adulthood inhibits HPT response to voluntary wheel running in a sex dependent manner, inhibiting lipolysis of WAT[2]. We evaluated the effect of chronic stress during adolescence on HPT axis response to voluntary exercise in adulthood[3], with emphasis on metabolic response in skeletal muscle and WAT. Wistar male and female rats (N=36 per sex) were divided in an undisturbed group (Control, C; n=18) and one chronic variable stress during adolescence group (CVS; n=18) (males: PND 30-70; females: PND 30-60). As adults (males: PND 84; females: PND: 74) rats were divided in: 1) exercise group: rats placed individually in a cage with a running wheel per 14 nights, 2) sedentary group with *ad libitum* feeding, 3) sedentary pair-fed group offered the same amount of food consumed by the exercised group, and kept in individual cages during 14 nights (6 rats/group). WAT weight was determined at sacrifice, hormones quantified by RIA and ELISA, gene expression by RT-PCR. Exercise-induced loss of fat mass was not detected in CVS rats. Exercise decreased corticosterone levels in C males and females of both treatments, supporting sex difference on HPA axis reprogramming by CVS. HPT axis response to voluntary exercise is attenuated by CVS also in a sex dimorphic manner: CVS decreased *Trh* expression in hypothalamic paraventricular nucleus and no changes in thyroid hormones concentration in males, whereas in females, slightly increased TSH, T4 and T3 levels. Sex also influenced the response of skeletal muscle and WAT to CVS. *Dio2* and *Pgc1a* slightly increased expression in skeletal muscle of males, not of females. *Adrb3* expression in WAT increased in females, but not in males; exercise-induced stimulation of *Hsl* expression was not observed in either sex after CVS. These results suggest that CVS imposed during rat adolescence inhibits the responses to voluntary exercise of HPT axis activity of thyroid hormone-targets in WAT and skeletal muscle in sex dependent

manner. These changes could lead to reduced mobilization and the utilization of energy fuels coincident with the fatigue observed after exercise in patients with subclinical or clinical hypothyroidism. (Funded: *CONACYT 284883, DGAPA IN213419*)[1]*Uribe, Endocrinology 155:2020-2030, 2014.* [2]*Parra, Front Endocrinol 10(418):1-13, 2019.*[3]*Parra, J Endocr Soc 4(Abstract Supp) Abstract SAT-451, 2020.*

Thyroid
THYROID HORMONE METABOLISM AND ACTION

Clinical and Sociodemographic Profile of Patients With Thyroid Storm: A National Inpatient Sample Database Analysis

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Background: Thyroid storm (TS) is a rare, life-threatening disease that is associated with significant mortality. The clinical outcome of these patients has not been evaluated in general practice on a national scale. Our study aimed to find the clinical characteristics and outcomes of patients admitted to community hospitals with TS using the National Inpatient Sample (NIS) database.

Methods: We conducted a retrospective study of adult patients (>=18 years of age) diagnosed with primary and secondary TS from the NIS database from 2012 to 2014. The NIS is the largest all-payer inpatient care database in the United States, containing data on more than seven million hospital stays each year. Statistical analysis performed included Chi-Square test, Wilcoxon two-sample test, Fisher's exact test and multiple logistic regression with a *p*-value<0.05 considered significant.

Results: In total, 2,163 hospitalizations with TS were identified. The incidence of TS in hospitalized patients was 11.96 per 100,000 hospitalizations. Compared to all other adult hospitalizations reported over the same period, admission with TS was significantly associated with a higher prevalence in African Americans (31.4% vs 14.7%, p<0.001) as well as concomitant blood diseases (31.4% vs 21.9%, p<0.001), drug use disorder (11.4% vs 8.4%, p<0.001), electrolyte disturbance (36.9% vs 23.8%, p<0.001), and psychosis (38.1% vs 28.5%, p<0.001). Admission with TS was associated with lower prevalence of concomitant cancer (2.5% vs 4.9%, p<0.001) and renal disease (5.6% vs 12.2%, p<0.001), along with a higher risk of death during hospitalization (3.9% vs 2.2%, p<0.001). There was no significant association between TS and GI disease, cardiovascular disease, pulmonary disease or rheumatoid arthritis. Admission with TS was associated with longer average length of stay (TS median: 4 days, Non-TS: 3 days, p<0.001) and higher total hospital charge (TS median: $27,360, Non-TS: $24,346, p<0.001). Additionally, TS had a higher incidence in urban populations with large hospitals.

Overall, inpatient mortality rate was 3.9%. For those with TS, the odds of inpatient death were greater for age group 30-59 compared to <30 (OR 2.916, p=0.026), age group >60 compared to <30 (OR 3.157, p=0.022), males (OR 2.20, p<0.001), those with cancer (OR 6.42, p<0.001), those with

electrolyte disturbance (OR 6.12, p<0.001) and those with a neurologic disorder (OR 2.46, p=0.002). Admitted patients with a concomitant psychological disorder had lower odds of death (OR 0.38, p=0.03).

Conclusions: This study identified clinical characteristics associated with TS-related admission including female gender, age 30-59, Caucasian race, and urban populations. Higher mortality was associated with patients 30-59 years and >60 years of age, electrolyte disturbances, blood disease, weight loss, paralysis, cancer, renal disease, and male gender.

Thyroid
THYROID HORMONE METABOLISM AND ACTION

Dio2-CreErt2 Knockin Model to Identify T3-Generating Cells That Express Type 2 Deiodinase in Tissues

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Background: Thyroid hormone promotes many developmental and homeostatic functions. Apart from adequate circulating levels, the concentration of the active hormone T3 within tissues may be amplified by type 2 deiodinase (Dio2) by conversion from the precursor T4. *Dio2* is critical in auditory development, bone maturation, brain function and control of the hypothalamic-pituitary-thyroid axis. Despite its crucial role, an obstacle to studying Dio2 is that the protein has a short half-life, is at low levels and is often transiently expressed, making it difficult to identify Dio2 in tissues at cellular resolution. **Methods:** We derived a Dio2-CreERt2 knockin mouse that expresses tamoxifen-dependent Cre recombinase from the endogenous *Dio2* gene. When crossed onto Ai6 reporter mice, following tamoxifen treatment, Dio2-CreERt2 expression is detected as fluorescent signal in specific cells in brain regions, pituitary, and other tissues. We showed previously that Dio2 is essential for hearing with rising expression levels in the cochlea prior to onset of hearing. The Dio2-CreERt2 model identified positive cell types in the cochlear spiral ligament, septal divisions and modiolus around the sensory epithelium. Dio2-positive fibrocytes were adjacent to and extended projections around blood capillary networks, the source of T4 supply. Transcriptome analysis of isolated positive cells revealed bone lineage-related origins for many of these cells. **Conclusion:** The Dio2-CreERt2 model detects Dio2 expression sensitively at cellular resolution. In the cochlea, Dio2-positive cell types reside in vascularized support tissues, suggesting combined endocrine and paracrine-like control of the T3 supply. Analysis of cell origins suggests novel interactions between endocrine and skeletal systems in promoting T3 action required for hearing.

Thyroid
THYROID HORMONE METABOLISM AND ACTION

Identification of Cell Types that Express Dio3 Deiodinase, a Thyroid Hormone-Inactivating Enzyme, Using a Dio3-CreERT2 Reporter System

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Background: Thyroid hormone promotes development, growth and metabolism. The level of thyroid hormone ligand (triiodothyronine, T3) in tissues depends not only on circulating levels but also upon tight regulation by activating and inactivating deiodinases within tissues. Type 3 deiodinase (Dio3) inactivates T3 and its precursor thyroxine (T4) and mediates many functions including in neurodevelopmental, sensory and reproductive systems. Dio3 is subject to genomic imprinting. Despite its critical functions, Dio3 is often expressed transiently and at low levels in restricted cell populations making it difficult to detect in natural tissues. **Methods:** To visualize Dio3 expression at cellular resolution, we derived a *Dio3*-CreERt2 knockin allele that expresses tamoxifen-dependent Cre recombinase from the endogenous *Dio3* gene. When crossed with Ai6 reporter mice, *Dio3*-CreERt2-positive cells display fluorescent signals. When tamoxifen-treated at neonatal ages, *Dio3*-CreERt2 recapitulates endogenous *Dio3* expression as previously reported in brain: in the bed nucleus of the stria terminalis and preoptic nuclei. In addition, we uncovered several positive cell groups in the hypothalamus, brain stem, pituitary and other tissues. Drastic differences were observed for *Dio3*-CreERt2 as a paternally versus maternally inherited allele, revealing imprinting effect in specific cell types. *Dio3*-CreERT2 activity is enhanced by T3 administration, in accordance with *Dio3* as a T3-indicible gene. **Conclusion:** The *Dio3*-CreERT2 model sensitively reveals Dio3-expressing cell types in tissues. The model is useful for studying expression patterns, imprinting and lineage tracing of Dio3-positive cells during development and homeostatic challenges.

Thyroid
THYROID HORMONE METABOLISM AND ACTION

iPSC-Derived Human Hepatocytes as a Novel Model to Investigate Thyroid Hormone Action and Signaling

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Thyroid hormone (TH) actions are essential to normal metabolism and neurologic function. Abnormal TH levels can lead to significant morbidity including metabolic abnormalities, cardiac disease, and obesity. TH action is mediated by the thyroid hormone receptor (TR) isoforms and their coregulators. In the disease models of Resistance to Thyroid Hormone (RTH) it is clear that the TR isoforms play tissue-specific roles in humans, however a platform for drug discovery to potentially treat the diseases does not exist. We hypothesize that human hepatocytes (iHeps) derived from induced pluripotent stem cells (iPSCs) will serve as an ideal model to study TH signaling and to delineate mechanisms of TH diseases in humans. To investigate the TH action in humans, we have developed a serum free human iPSC hepatic differentiation protocol that utilizes sequential exposure to growth factors to mimic actual