

MON-042

Exercise may improve cardiometabolic, reproductive and psychological outcomes in women with Polycystic Ovary Syndrome (PCOS). Clinical Practice Guidelines recommend exercise to treat PCOS, but the most effective exercise prescription is unclear. The aim of this randomized controlled trial was to evaluate the effects of six months of thrice weekly high-intensity interval training (HIIT) and continuous aerobic exercise training (CAET) programs compared with no exercise in previously-inactive women aged 18–40 years with PCOS. The primary outcome was change in ovulation rate. Ovulation was assessed with daily at home ovulation prediction kits, and confirmed with serum progesterone levels. Fisher's exact test was used to compare groups. Secondary outcomes included change in BMI, waist circumference, blood pressure, A1C, fasting glucose, fasting insulin, and lipids and were analyzed using repeated measures mixed models. 47 women were randomly assigned to no exercise control (n=17), HIIT (n=16), or CAET (n=14). 22/33 (66.7%) women ovulated during the intervention period: no exercise: 8/12 (66.7%), HIIT: 8/11 (72.7%), and CAET: 6/10 (60%); NS between groups. BMI decreased significantly in the CAET group compared with control (-1 kg/m^2 , $p=0.01$) and compared with HIIT (-0.9 kg/m^2 , $p=0.04$). Mean waist circumference decreased significantly in all groups with no significant difference between groups. There were no significant within- or between- group changes for body weight. No within- or between group differences were identified for mean blood pressure, A1C, fasting glucose, fasting insulin, or triglycerides. Mean LDL-C was significantly different between the HIIT and CAET groups (-0.33 mmol/L , $p=0.03$), as LDL-C decreased in the HIIT group but not in the CAET group. HDL-C increased in the HIIT group compared with the no exercise group (0.18 mmol/L , $p=0.04$), with no significant difference between the CAET and no exercise groups ($p=0.47$). In conclusion, CAET and HIIT interventions in women with PCOS did not affect ovulation rates. CAET and HIIT both were effective at improving anthropometrics and some cardiometabolic health markers in women with PCOS. Further studies are needed to determine optimal exercise prescriptions for reproductive, anthropometric and cardiometabolic outcomes in women with PCOS.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Resolution of a Cystic Macroprolactinoma with Dopamine Agonist Therapy

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Background. Prolactinomas with cystic regions occupying $\geq 50\%$ of tumor volume are classified as cystic prolactinomas.

They appear to arise from tumor necrosis or hemorrhage. Though Pituitary Society guidelines recommend surgery as first-line treatment for cystic prolactinomas, there is evidence that cystic prolactinomas are hormonally and anatomically responsive to treatment with dopamine agonists (DA). We present a case of a cystic macroprolactinoma fully responding to treatment with cabergoline. **Case.** A 31 year old male was referred for evaluation of gynecomastia, diminished libido, and erectile dysfunction that occurred over the course of eight months. Bilateral glandular breast tissue with a slight right asymmetry was present. Testes were 15–20 mL, soft, and without masses. Phallus and pubic hair were unremarkable. Morning (8 AM) testosterone, estradiol, and LH levels were 92 ng/dL (348–1197), 13.4 pg/mL (7.6–42.6), and 2.0 mIU/mL (1.7–8.6), respectively. Prolactin level was 331 ng/mL (4–15), and MRI with pituitary protocol revealed a 1.4 x 1.0 x 1.5 cm cystic mass with peripheral rim enhancement and extension into the suprasellar cistern. No mass effect on the optic chiasm was observed. Somatotroph, thyrotroph, and corticotroph axes were unaffected. Cystic macroprolactinoma causing hyponadotropic hypogonadism complicated by gynecomastia was diagnosed. The patient chose initial management with cabergoline 0.25 mg twice weekly. Three months after starting treatment, libido and erectile function had recovered to baseline, 8 AM testosterone was 607 ng/dL, and hyperprolactinemia was well controlled (4.2 ng/mL). At six months, anatomic resolution of the cystic macroprolactinoma was demonstrated on repeat pituitary MRI. Plastic surgery was required for management of gynecomastia. **Conclusions.** Surgery is recommended for management of cystic prolactinomas due to concern that a lack of dopamine receptors in the cystic components of tumors will make DA ineffective reducing tumor size. However, this case joins a growing body of evidence that DA can treat hyperprolactinemia and induce regression of cystic macroprolactinomas. For example, in a retrospective case review of patients with cystic macroprolactinomas at Massachusetts General Hospital, persistent cyst reduction occurred in 20 of 22 patients treated initially with DA, and median reduction in cyst volume exceeded 80 percent. Median time to documented cyst reduction was approximately six months, and there was no difference in degree of cyst reduction for patients treated with bromocriptine or cabergoline. The response of cystic prolactinomas to DA is similar to solid prolactinomas, and DA are reasonable initial treatment for cystic macroprolactinomas without clear indications for surgery.

Thyroid**THYROID NEOPLASIA AND CANCER**

TRK-Fusion Thyroid Cancer: A Clinical Overview in a Large Population at a Single Cancer Center

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MON-491

Introduction: Most thyroid cancers (TC) are due to mutually exclusive somatic driver mutations. *NTRK* fusions are rare oncogenic drivers in papillary TC (PTC), poorly differentiated TC (PDTC) and anaplastic TC (ATC), estimated to be in 2.3% of all TC. However, the clinical presentation and behavior of TRK-fusion TC remains largely unknown. **Methods / Case Presentation:** Using institutional databases, we identified all TC patients (pts) with an *NTRK* fusion reported on somatic testing performed by a CLIA-certified laboratory. Data from the medical records were collected. The objective of this study was to investigate the clinical and pathological features of TC pts whose tumors harbored an *NTRK* fusion. **Results / Discussion:** We identified 36 TC pts with somatic *NTRK* fusions. Fusion testing was generally done in pts with advanced or radioactive iodine refractory (RAI-R) disease. Median age at diagnosis was 27.4 years (range 4–75 years), 21 (58%) were female and 16 (44%) were pediatric. 28/36 (78%) pts had PTC, 2/36 (5%) PDTC and 6/36 (17%) ATC. There were a total of 12 (33%) *NTRK1*, 24 (67%) *NTRK3*, and no *NTRK2* fusions. In ATC and PDTC pts *NTRK3* was the most common *NTRK* fusion 7/8 (87%). In PTC pts, 11 (39%) had *NTRK1* and 17 (61%) had *NTRK3*. In the adult pts *NTRK3* was more common 17/20 (85%) (Odds Ratio 7.2, P=0.013), however, in pediatric pts rate of *NTRK1* and *NTRK3* were similar. One pt had additional mutations along with the *NTRK* fusion, an ATC pt with multiple mutations including *BRAF* V600E. Of the 30 PTC/PDTC pts, 23 (77%) had distant metastases (mets). 14 (38%) pts had distant mets at diagnosis and 11 (69%) pediatric pts had distant mets. Lung 21 (70%) and bone 9 (30%) were the most common distant mets sites. In the PTC pts with distant mets, 9 (41%) had RAI-avid and 11 (50%) had RAI-R disease. In the entire cohort of 36 pts, 17 (53%) were on a systemic therapy of whom 11 pts were PTC. *NTRK* directed was the most common systemic therapy 16 (94%). All PTC pts were alive with a median time from diagnosis of 46 months (Interquartile 1–3: 25–118 months). Four ATC and one PDTC pts had died at the time of the analysis. **Conclusions:** In this study we confirmed that *NTRK* fusions occur primarily in PTC but also in less differentiated tumors. Most were young pts but *NTRK* fusions were identified in tumors from adults as old as 75 years. *NTRK1* and *NTRK3* were the most common *NTRK* fusions with *NTRK3* being more common in adults. In thyrocyte-derived TC pts, *NTRK* fusions are mutually exclusive genetic events that occur in pts of all ages and varying histologies. Given the availability of *NTRK* targeted therapy, consideration should be given to testing for *NTRK* fusions in advanced thyroid cancer pts, especially those in whom prior genetic testing did not identify an oncogenic driver.

Adipose Tissue, Appetite, and Obesity**NEURAL MECHANISMS OF OBESITY****Characterization of Dual Projection Patterns of Refeeding-Activated Neurons in the Paraventricular Nucleus**

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SAT-605

We have observed that following a fast, animals terminate their food intake within 2h after refeeding accompanied by a pattern of neuronal activation as identified by c-fos immunostaining that involves a number of brain regions associated with the regulation of food intake including the nucleus tractus solitarius (NTS), parabrachial nucleus (PBN), central nucleus of the amygdala (CEA), hypothalamic arcuate and paraventricular nuclei, and bed nucleus of the stria terminalis. We also observed striking c-fos activation in the posterior-lateral hypothalamus called the paraventricular nucleus or PSTN, raising the possibility that it may also be an important anorectic center in the brain. To establish how the PSTN is integrated into the CNS, we performed dual-label retrograde tract tracing studies to characterize whether refeeding-activated PSTN neurons project to one, or more than one target area in the CNS. Adult, Sprague-Dawley rats received dual stereotaxic injections of Alexa Fluor 488- and Alexa Fluor 555-conjugated cholera toxin β subunit (CTB; 0.1%, 0.5–1 μ l volume) into the 1) PBN and NTS, 2) PBN and CEA and 3) NTS and CEA. After 7–12 days, the animals were fasted for 24 h and then given free access to food for 2 h before euthanasia by transcardial perfusion with 4% paraformaldehyde. Brains with successful dual injections were further processed for c-fos immunohistochemistry. The results showed that 26.5 \pm 3.8% of PSTN neurons projecting to the PBN also project to the CEA, and 34.6 \pm 7.6% of PSTN neurons that project to the CEA also project to the PBN. In addition, 20.2 \pm 2.7% of PSTN neurons that project to the PBN also project to the NTS, and 38.1 \pm 9.7% of PSTN neurons that project to the NTS also project to the PBN. Furthermore, 35.0 \pm 12.5% of PSTN neurons that project to the CEA project to the NTS and 37.1 \pm 4.0% of PSTN neurons that project to the NTS project to the CEA. Finally, up to 15% of the neurons with dual projections to the PBN and CEA contained c-fos after refeeding; up to 18% of the neurons with dual projections to the PBN and NTS contained c-fos; and up to 30% of neurons with dual projections to the NTS and CEA contained c-fos. We conclude that a large number of PSTN neurons have more than one projection site within the brain, thus the PSTN appears to have the capability of simultaneously communicating information about appetite to several, major feeding-related sites within the brain, presumably to terminate feeding.

Neuroendocrinology and Pituitary**HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION****Chronic Treatment Of Juvenile Hypothalamic Pomc-deficient Mice With RM-493 Prevents The Development Of Obesity**

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Arc-*Pomc* knockout mice have a disruption of the two neural enhancers for the *Pomc* (proopiomelanocortin) gene, resulting in selective loss of *Pomc* gene expression in the