loss of the proximal row of carpal bones. His mother was followed as an adolescent with presumed juvenile rheumatoid arthritis. Genetic testing confirmed MAFB gene mutation (c.206C>T,p.Ser69Leu) in both patient and mother. At 7y, skeletal survey showed diffuse osteopenia and mild height loss in T1. DXA (L1-4) Z-score was -0.7. Calcium phosphate metabolism indices were within reference ranges. Bone Specific Alk Pi was modestly increased and C-telopeptide markedly increased.He received Denosumab (0.5-0.75 mg/Kg) 4-monthly for two years and experienced less pain and increased daily activities with improved R wrist function. Osteolysis stabilized and none was noted in the L wrist or ankles. BMD Z-score was -0.2. A year following treatment (2016) he received two more injections of Denosumab following pain and movement restriction of R elbow, R knee and L ankle. In 2019 (13y) he fell and radiology showed, R knee osteopenia, R wrist almost complete destruction of the carpal bones. Neither ankle nor L wrist showed osteolysis. R upper limb musculature was wasted when compared with the left. Shoulder and elbow strength were preserved. BMD Z-score was -1.2. Serum calcium, 25(OH)Vitamin D and PTH were normal. Bone specific alkaline phosphatase and C-Telopeptide were elevated. Serum creatinine was normal, eGFR 150 ml/min/1.73m2, ACR (6.6 [normal< 3.5] mg/mmol)) with no hypercalciuria or nephrocalcinosis. He was normotensive.High resolution peripheral quantitative computerized tomography (HRpQCT) of the L distal radius and distal tibia compared with 7 age-matched healthy males showed reduced total volumetric BMD (186.4;198.2-306.4), normal trabecular volumetric BMD and markedly reduced cortical volumetric BMD (320.4;636.5-792.5). Cortical thickness was below the expected range. HRpQCT measurements of the R wrist and tibia were similar. sRANKL, 6 weeks after Denosumab were markedly increased in both undiluted (35.4 pmol/L) and averaged diluted samples (83.73 pmol/L) when compared with healthy age-matched children (0.21-0.41pmol/L).

Conclusions/Clinical Lessons:MCTO (MAFB, mutation c.206C>T,p.Ser69Leu), has a generalized high turnover skeletal phenotype (osteoporosis), likely driven by very high levels of sRANKL. Denosumab is a targeted treatment for the osteoporosis, which may help stabilize the osteolysis.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Chronic Exposure to Predator Odour Stress Disrupts LH Pulsatility and Delays Puberty While Activation of Amygdala Kisspeptin Advances Puberty

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Chronic exposure to predator odour stress disrupts LH pulsatility and delays puberty whileactivation of amygdala kisspeptin advances pubertyDeyana Ivanova MS[1], Xiao Feng Li MD/PhD[1], Caitlin Mcintyre BS[1], and Kevin O'Byrne PhD[1];[1]Department of Women and Children's Health, Faculty of Life Science and Medicine, King'sCollege London, UKPost-traumatic stress (PTSD) is associated with altered pubertal timing and predator odourexposure is a classical rodent PTSD model. Kisspeptin neurones in the posterodorsal sub-nucleus of the medial amygdala (MePD) are thought to modulate pubertal timing and anxiety.We test the hypothesis that psychosocial stress, processed by the MePD, is relayed to theGnRH pulse generator to delay puberty. Female mice were exposed to predator odour, 2,4,5-Trimethylthiazole (TMT), for 14 days from postnatal day (pnd) 21 and pubertal onset wasmonitored. Anxiety was tested using the Elevated Plus Maze (EPM), Light/Dark Box (LDB) andsocial interaction (SI). The effect of TMT on luteinizing hormone (LH) pulses was measured,on pnd 26 and 29. Additionally, kisspeptin-cre mice were bilaterally injected with hM3Dq-DREADD AAV in the MePD at pnd 13. From pnd 21, CNO was administered via drinking waterfor 14 days and pubertal onset was monitored. The TMT-mice showed a significant delay offirst estrous (FE; TMT: 38.1 ± 0.5 vs. control: 33.3 ± 0.6 days; $p<0.0001$; n=10-14) withoutaffecting body weight (BW; $p=0.9$; n=10-14). TMT-mice spent less time exploring the openarm of the EPM (TMT: 13 ± 3 vs. control: 32 ± 5 secs; $p<0.05$; n=10-14) and in the lightcompartment of the LDB (TMT: 117 ± 12 vs. control: 162 ± 15 secs; $p<0.05$; n=10-14), whileengaging less in SI (TMT: 26.8 ± 2.8 vs. control: 47.7 ± 8.8 secs; $p<0.05$; n=10-14) during TMT-exposure compared to controls. The TMT group exhibited a reduction in LH pulse frequencyon pnd 26 (TMT: 0.2 ± 0.2 vs. control: 1.7 ± 0.4 pulses/2 h; $p<0.05$; n=6-9) and 29 (TMT: 0.6 ±0.2 vs. control: 2.6 ± 0.4 pulses/2 h; $p<0.001$; n=6-9). DREADD activation of kisspeptinneurones in the MePD advances FE (DREADD: 30 ± 1 vs. control 34.67 ± 0.82 days; $p<0.05$;n=6) without affecting BW ($p=0.9$; n=6). Predator odour stress reduces GnRH pulse generatorfrequency, delays puberty and enhances anxiety-like behaviour, while selective chemogeneticactivation of kisspeptin neurones in the MePD advances puberty in female mice.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Treat: A Randomized Controlled Trial Examining the Effects of Time Restricted Eating on Weight Loss and Metabolic Markers

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Background: Studies indicate that time-restricted eating (TRE) can prevent weight gain and/or lead to weight loss [1,2]. The few human studies to date are small and/or non-randomized