Methods: Patients treated with thyroid surgery for benign disease (n=425) or radioactive iodine for hyperthyroidism (n=1637) at a single tertiary institution between 2000 and 2017 were invited to complete a validated thyroid-specific QoL instrument (City of Hope), reporting scores 0–10, where higher scores are associated with greater QoL. Responses were received from 307 patients, of whom 114 (37%) had Graves' disease, treated with total thyroidectomy (n=23) or doses of 15mCi (550MBq) radioiodine (n=91, including 19 patients receiving 2 or more doses). The results of patients with Graves' disease are reported here. Medians [interquartile ranges] are compared with the Mann-Whitney test (alpha 0.05).
Results: 85% of respondents were female, with no difference in gender between groups (p=0.11). Thyroidectomy patients were more likely to be younger (36 [31–49] vs 50 [39–59] years, p=0.004); and have a shorter duration between treatment and survey (5.9 [2.4–9.6] vs 7.6 [4.9–11.6] years, p=0.04). No overall QoL deficit was seen in patients treated with surgery compared to radioiodine (6.8 [5.2–7.3] vs 7.0 [5.8–8.1], p=0.08). However, patients treated with surgery reported reduce QoL in psychological (6.6 [4.7–7.5] vs 7.0 [5.9–8.2] p=0.05) and social (7.9 [6.4 – 8.9] vs 8.9 [7.4–9.8] p=0.01) subdomains compared to radioiodine-only treated patients. Within the social subdomain, the QoL detriment was driven by lower scores relating to questions regarding impact on personal and family relationships, support, and isolation (p<0.001), and not by impact on activities of daily living or employment concerns. Interestingly, there was no between group difference in the physical symptom subdomain (p=0.16). QoL differences between treatment modalities were preserved when patients receiving multiple doses of radioiodine were excluded.
Discussion In this non-randomised cross-sectional study from a tertiary-hospital population in Australia, a QoL deficit was demonstrable in subdomain scores for patients with Graves' disease treated with surgery compared to radioiodine, although the overall result was not significantly different. Better understanding of patient experiences is required to guide treatment strategies and appropriately counsel patients.
References (1) Torring et al. Thyroid. 2019;29(3):322–31. (2) Abraham-Nordling et al. Thyroid. 2005;15(11):1279–86. (3) Ljunggren et al. Thyroid. 1998;8(8):653–9.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

TSH/TSHR Signaling Deficiency Impairs Spatial Learning and Memory

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Background: Subclinical hyperthyroidism is associated with cognitive impairment, but the mechanism has remained unclear. As subclinical hyperthyroidism is characterized by significantly decreased TSH levels, this study aimed to investigate whether TSH regulates cognitive function. **Methods:** The correlation between TSH and cognitive impairment was investigated in a cross-sectional population study. The role of TSH/TSH receptor (TSHR) signaling in spatial learning and memory was further examined by behavior tests in *Tshr*$^{-/-}$ mice. Dendritic spine, synaptic density and structure of hippocampal CA1 pyramidal neurons were detected by Golgi's method and electron microscopy. The mRNA and protein expression levels of learning and memory-related genes were assessed by RNA sequencing, real-time PCR, immunoblotting and immunofluorescence approaches. **Results:** Serum TSH level correlated negatively with cognitive impairment in the current population. Consistently, *Tshr* deletion in mice led to significantly compromised performance in hippocampus-dependent tasks, reduced dendritic spine density and excitatory synaptic density as well as altered synaptic structure in CA1 subfield of the hippocampus. Furthermore, the mRNA levels of learning and memory-related genes were altered, and protein levels of CREB-regulated genes were downregulated in the hippocampus of *Tshr*$^{-/-}$ mice. **Conclusions:** These findings reveal that TSH/TSHR signaling ablation impairs spatial learning and memory, indicating a decline in TSH level might contribute to the increased prevalence of cognitive impairment in subclinical hyperthyroidism patients.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Neonatal Severe Hyperparathyroidism: Extreme Hypercalcemia as a Robust Marker for Homozygous Dosage of Pathogenic CASR Variants

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SUN-366

Context: Neonatal severe hyperparathyroidism (NSHPT) is a rare and life-threatening emergency. It includes generalized hyperparathyroid bone disease and respiratory distress from combinations among a narrowed thorax, rib fractures, hypotonia, and biochemical disturbances. Successful therapy is compatible with long life and a healthy prognosis. However, neuromotor retardation may persist after otherwise successful therapy. The time and amplitude of hypercalcemia likely correlate with irreversible neuromotor retardation; thus, early intervention seems critical in many cases. NSHPT is usually caused by homozygous or heterozygous pathogenic variant(s) of the *CASR*; a heterozygous variant of this gene is also the usual cause of familial hypocalciuric hypercalcemia (FHH or FHH1). Homozygotes and heterozygotes with NSHPT are often not distinguished in the current literature. In theory, their management should differ. Optimum treatment in homozygotes is early total parathyroidectomy with induction of postoperative hypoparathyroidism. Optimal management of heterozygotes is more complex. It consists in temporizing measures and varies from careful observation without surgery, to bisphosphonates and/or calcimimetics, and to subtotal parathyroidectomy. The heterozygotes can then develop into healthy babies with asymptomatic FHH1. Evidence Acquisition: Each case met strict criteria for "severe" and neonatal disease. We analyzed the core