

## **Dr. Marcella Walker**

Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by hypercalcemia and elevated parathyroid hormone. Many patients with PHPT report symptoms such as fatigue, cognitive impairment, intellectual weariness, depression and anxiety. Data regarding the causal association of such symptoms with PHPT and their reversibility after PHPT is cured by parathyroidectomy (PTX) are insufficient. Therefore, it is unclear whether these complaints should be an indication for PTX. The field has been mired by studies that are small, inadequately controlled, or lack validated objective measures. Currently, both PHPT patients and clinicians are frustrated by the lack of clear evidence regarding the effects of PHPT upon cognition and improvement after PTX. Obtaining data that brings clarity to this issue is thus of considerable public health importance. Studies are needed to evaluate new tools to determine which are efficacious in objectively and consistently detecting cognitive changes in this specific population. Multimodal functional magnetic resonance imaging (fMRI) of the brain represents a technique that holds promise to objectively measure the cognitive changes that may accompany PHPT as well as their reversibility after surgical cure. Our preliminary data suggests there are several aspects of cognition that are affected by PHPT, including verbal memory, non-verbal abstraction, response speed and visual attention. To lay the groundwork for a well-controlled R01, we need to demonstrate that multimodal fMRI can detect changes in brain regions responsible for verbal memory, non-verbal abstraction, response speed, and visual attention. In addition, demonstration that multimodal fMRI findings correlate with post-PTX improvements in cognitive testing and the cardinal biochemical abnormalities of PHPT, serum calcium and parathyroid hormone levels, would provide further support for a causal relationship. We propose to study postmenopausal women with PHPT undergoing PTX before and 6 months after surgery to 1) determine whether there are post-parathyroidectomy changes in neuroactivation on multimodal fMRI during performance of tasks corresponding to verbal memory, non-verbal abstraction, response speed and visual attention; and 2) determine if any observed neurofunctional changes are associated with post-parathyroidectomy improvement in PTH concentration or serum calcium levels. There is a clear need for further studies in this area to help guide clinicians in the management of PHPT patients who manifest cognitive and psychiatric symptoms. This study will lay the groundwork for a larger well-controlled R01 application to the NIH to further utilize multimodal fMRI to map cognitive changes in PHPT and other disorders of parathyroid gland dysfunction.