

## **Frontal Gray Matter Reduction After Breast Cancer Chemotherapy and Association With Executive Symptoms: A Replication and Extension Study**

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Cognitive changes related to cancer and its treatment have been intensely studied, and neuroimaging has begun to demonstrate brain correlates of these changes. We recently reported structural brain changes in a prospective longitudinal cohort of breast cancer patients. Decreased gray matter density, particularly in frontal regions, was detected one month after completion of chemotherapy and partially recovered over the next year. These findings helped confirm a neural basis for the cognitive symptoms reported by many prior studies, which most commonly involve executive and memory processes in which the frontal lobes are a critical component of underlying neural circuitry. Here we present data from an independent, larger and more demographically diverse cohort that is more generalizable to the breast cancer population. 3.0T MP-RAGE structural MRI scans were acquired on 27 breast cancer patients treated with chemotherapy, 28 breast cancer patients not treated with chemotherapy, and 24 matched healthy controls (all participants were female). Study measures were completed at baseline (after surgery but before radiation, chemotherapy, and/or anti-estrogen treatment) and one month following the completion of chemotherapy, or yoked intervals for the non-chemotherapy and control groups. Gray matter density was examined using optimized voxel-based morphometry (VBM) methods. Results showed decreased frontal gray matter after chemotherapy, as observed in our initial cohort, which was accompanied by self-reported difficulties in executive functioning. These findings provide confirmatory evidence of frontal morphometric changes that may be a pathophysiological basis for cancer and treatment-related cognitive dysfunction. Ongoing research into individual risk factors for such changes will be critical for development of treatment and prevention strategies.