Functional Connectivity and Arterial Spin Labeling in Chemotherapy Induced Cognitive Impairment ("Chemobrain")

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INTRODUCTION

Chemobrain (CB) is a neurological disorder resulting from the systematic treatment of cancer using chemotherapy. Cognitive deficits such as lack of concentration, short term memory loss and foggy thinking[1] are symptoms. Though it is a well-described disorder in clinical practice, little research has been done to quantify functional disruptions in patient's brains using MRI and fMRI. Given these symptoms emulate other disorders such as attention deficit disorder (ADD) and mild cognitive impairment (MCI), which have benefitted from evaluation by functional MRI techniques, we hypothesize that the evaluation of chemobrain may likewise benefit. In particular, resting state functional connectivity MRI (rs-fcMRI) has recently been shown to measure robust memory and attentional networks in humans [2]. These networks are disrupted in ADD [3] and MCI [4], and this study seeks to provide a proof of concept case study by measuring functional network changes using rs-fcMRI and arterial spin labeling (ASL) pre and post chemotherapy.

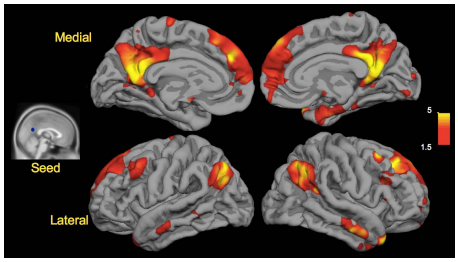

Figure 1. Functional connectivity pattern with a posterior cingulate seed region in Controls.

METHODS

Resting state fMRI and ASL data were collected on five control subjects and one patient pre and 3 months post-chemotherapy. ***Rs-fcMRI*** data was motion corrected, normalized to template space, spatially smoothed, and temporally band pass filtered. Signals from the lateral ventricles, deep white matter, and whole brain mask were regressed out on a voxel by voxel basis as physiological noise. Signal from a seed region in the posterior cingulate (PCC) was used as a regressor of interest to isolate regions functionally correlated [5,6]. This procedure was done on 5 control subjects (fig 1) and two time points of a CB patient, pre and post-chemo. Correlation coefficients were then transformed to Fischer Z values for group analyses. ***ASL*** data was motion corrected and delta M, the change in magnetization, was calculated. A two-sample t-test compared control vs. CB time points for both rs-fcMRI and ASL.

RESULTS

Functional connectivity between the posterior cingulate and the medial temporal cortex (MTL) and hippocampus (HF), regions known to be involved in memory, become increasingly disrupted post-chemo (fig 2B) ($p<0.005$). Changes were also measured in connectivity between the PCC and the anterior cingulate, known to be involved in working memory and attention ($p<0.001$). Also, CBF decreases in the lateral parietal cortex, and precuneus ($p<0.001$), and by 1.3% globally.

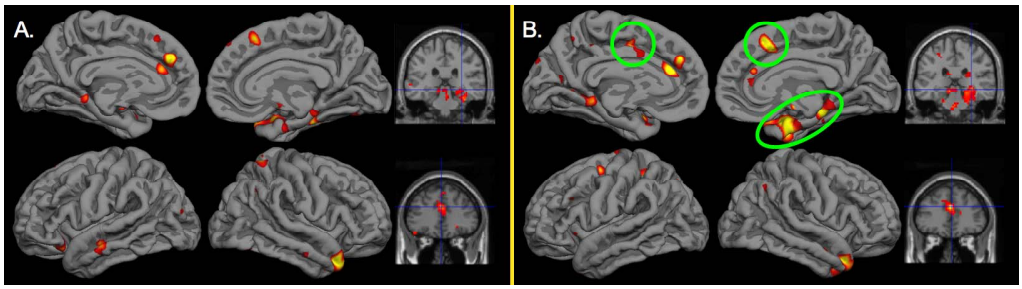

Figure 2. Results of resting state connectivity differences, controls vs. chemobrain. (**A.**) Baseline differences in CB prior to chemotherapy. (**B.**) Post-chemo differences in connectivity CB vs. controls. Results show an increased disconnect between the medial temporal cortex, hippocampus (HF), and marked differences in the anterior cingulate.

DISCUSSION

This case study sought to isolate functional changes in the brain caused by chemotherapy. Changes were found in connections between the PCC and the HF and medial temporal cortex, regions essential in memory, and between the PCC and anterior cingulate, essential for working memory and attention. CBF changes were measured globally, and within the supramarginal gyrus, and precuneus, regions associated with the HF and PCC through the default network [2]. These changes explain, in part, symptoms of memory loss, and lack of concentration suffered in chemobrain. Further longitudinal studies must be performed with larger group sizes, but this analysis shows that chemobrain cognitive changes can be measured even at the single subject level.

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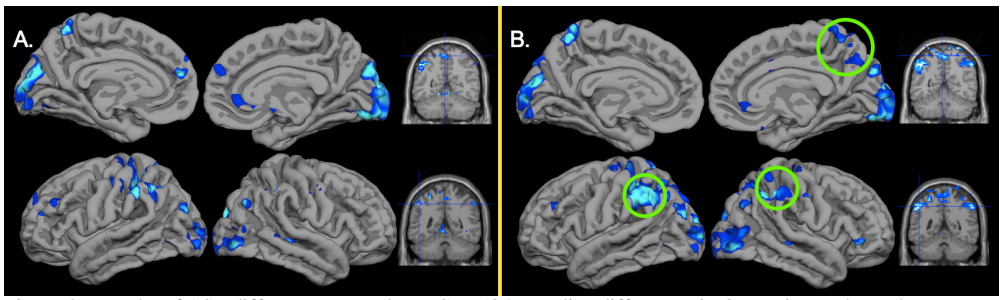

Figure 3. Results of ASL differences controls vs. CB. (**A.**) Baseline differences in CBF prior to chemotherapy. (**B.**) Post-chemo differences in CBF CB vs. controls. Results show decreased CBF in bilateral supramarginal gyrus, as well as dorsal precuneus, regions known to be involved in the default mode network [6].

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