Defining and Characterizing GWI Pathobiology using Longitudinal Brain Imaging Biomarkers

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BACKGROUND

Veterans of the 1991 Gulf War (GW) continue to experience chronic symptoms of Gulf War Illness (GWI) which includes fatigue, memory and concentration problems, muscle and joint pain and headaches. White matter changes have been correlated with neurotoxicant exposures during the war in GW veterans, including the acetylcholinergic inhibiting (AChEi) nerve agent sarin and similarly acting pesticides.

WM is highly susceptible to lipophilic neurotoxicants because it is made up of nearly 80% lipids. It is unknown if these WM changes are progressive over time and getting worse as veterans age and are less able to compensate for them or if GWI has become a progressive neurodegenerative disorder outside of normal aging parameters.

Answering these questions with longitudinal brain imaging and behavioral correlation analyses is crucial to determining appropriate treatment strategies based on the true course of the disorder.

BACKGROUND

The objective of this study is to assess if longitudinal brain volumetric changes are present in veterans with Gulf War Illness

We hypothesized that veterans with GWI would have longitudinal patterns of decreased brain volumetrics and white matter structural integrity.

METHODS

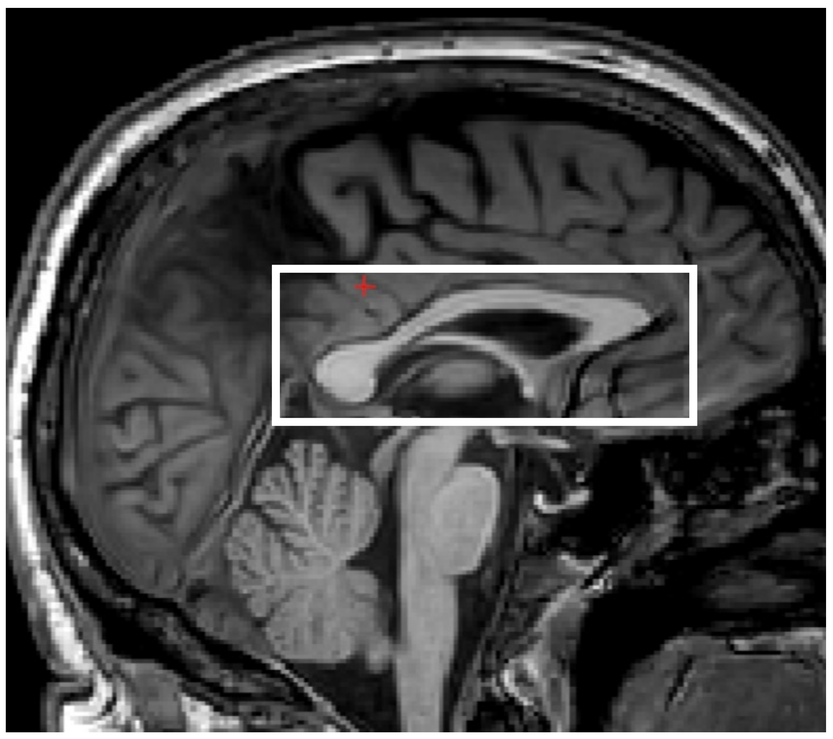
Study participants included 25 Gulf War veterans who met criteria for GWI based on the Kansas GWI definition. Each participant had MRI brain imaging performed at two time points on average five years apart on a Philips 3T scanner. The mean current age for participants was 56.5 years and included 38% women.

For this study, longitudinal Time 1 and Time 2 MPRAGE MRI scans were compared. Cortical reconstruction and volumetric segmentation were performed with Freesurfer 6.0, which is documented and freely available for download. Paired t-tests were performed to evaluate changes in brain volumetrics over time within the same individuals.

TABLE 1. Demographics

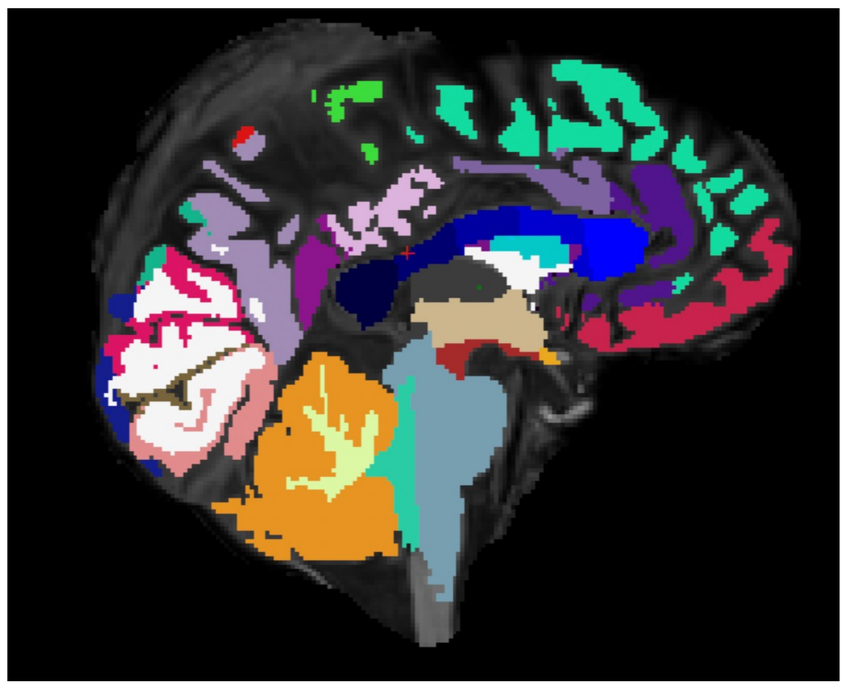
	Total (n = 25)
Age at T2, years: Mean (SD)	56.5 (4.7)
Sex: % Female	38%
Education, years: Mean (SD)	15.2 (1.9)
Race: n (%)	
White / Caucasian	19 (76%)
Black / African American	4 (16%)
Asian / Pacific Islander	1 (4%)
Multiracial	1 (4%)

FIGURE 1. Participant with GWI



Mid-sagittal slice showing the corpus callosum (CC)

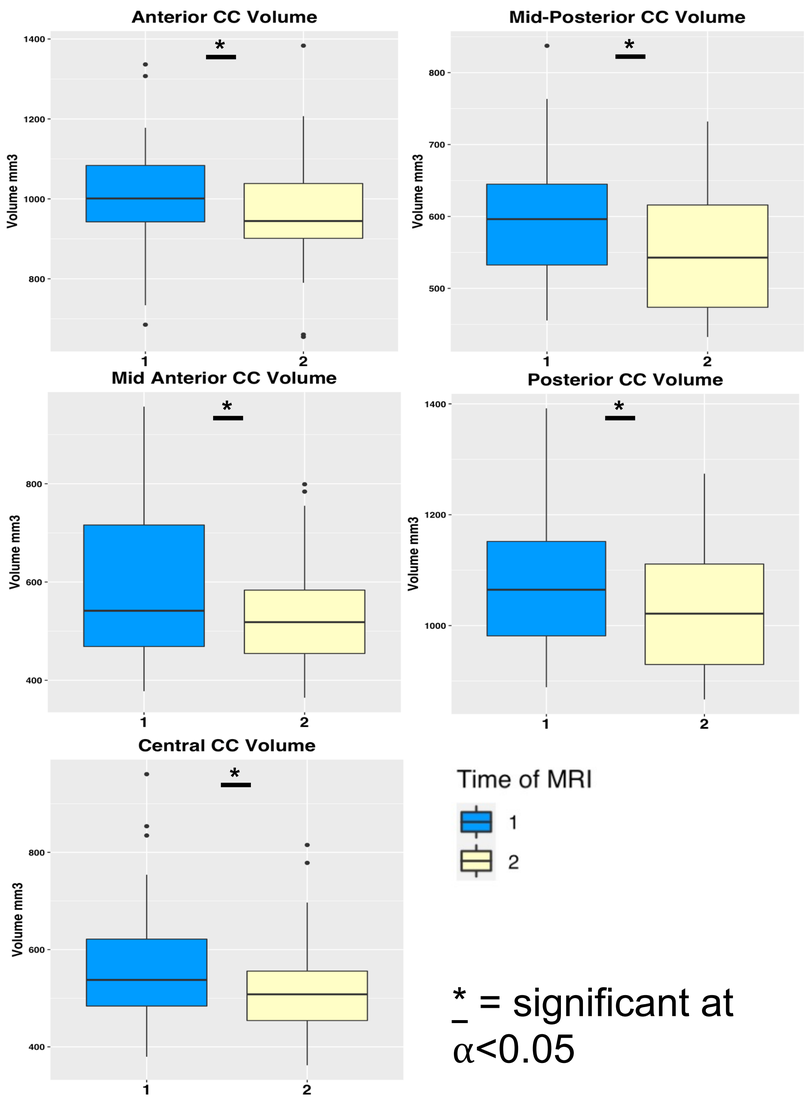
FIGURE 2. Freesurfer segmentation of CC



RESULTS

Veterans with GWI showed changes over time within a key white matter pathway, the corpus callosum. The corpus callosum was affected across all segmented regions. There were significant volume reductions in the anterior region (p=0.013), mid-anterior region (p=0.017), central region (p= 0.010), mid-posterior region (p= 0.002), and the posterior region (p=0.009) from Time 1 to Time 2.

FIGURE 3. Segmented CC Volumetrics



CONCLUSIONS

As hypothesized, individuals with GWI showed decreased volumetrics in a key white matter pathway over time. These white matter changes appear to be progressing as veterans' age. We have also noted cognitive changes in memory, attention and processing speed that may correlate with these brain volumetric changes.

More research is needed in a larger study sample to confirm these preliminary longitudinal brain imaging results and to compare with cognitive outcomes.

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