A Long-Term Longitudinal Examination of Brain Volume Change and Cognitive Functioning in Moderate to Severe Traumatic Brain Injury

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BACKGROUND

Voxel based morphometry (VBM) is a useful statistical method that allows researchers to quantify the volume of gray and white matter tissues in the brain. The use of volumetrics has been helpful in expanding the knowledge of the structural consequences that follow moderate and severe traumatic brain injury (TBI). It has been established that adults with TBI experience a loss of brain volume over time (Bendlin, et al., 2008), and importantly, these losses are related to cognitive functioning (Bigler, 2001). Although changes in brain volume during periods of acute recovery immediately following the injury have been documented, less is known about the course and consequence of change that occurs over longer periods of time. In this study, VBM was used to longitudinally investigate structural change occurring from 3 months to an average of 48 months after moderate to severe injury, and to determine the influence of these changes on long-term cognitive outcome.

Aims:

1. The study will track and quantify the amount of change in brain volume at four timepoints after injury, the last being a long term follow up at 48 months post injury.
2. The study will investigate the degree to which the amount of change occurring over time is related to long term cognitive functioning.

References:

Bendlin, B.B., Ries, M.L., Lazar, M., Alexander, A.L., Dempsey, R.J., Rowley, H.A., Sherman, J.E., & Johnson, S.C. (2008). Longitudinal changes in patients with traumatic brain injury assessed with diffusion-tensor and volumetric imaging. *Neuroimage, 42*, 503-514.

Bigler, E.D. (2001). Quantitative magnetic resonance imaging in traumatic brain injury. *J Head Trauma Rehabil, 16*(2), 117-134.

METHODS

- 7 participants with moderate to severe TBI were recruited.
- T1structural images were acquired from a 3T scanner at 4 timepoints: 3, 6, 12, and an average of 48 months post injury.
- Imaging data was pre-processed and analyzed using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm/) and SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/).
- Participants completed tests of working memory (Digit Span), visual scanning (Trails A), and executive functioning (Trails B and Stroop Color Word Test) at the last timepoint.

Participant Demographics

Participant	Age (years)	Education(years)	GCS Score
1	44	12	6
2	63	13	5
3	20	15	11
4	22	14	4
5	58	12	14*
6	26	12	8
7	22	16	8
Total Average	36.4(18.4)	13.4(1.6)	8(3.5)

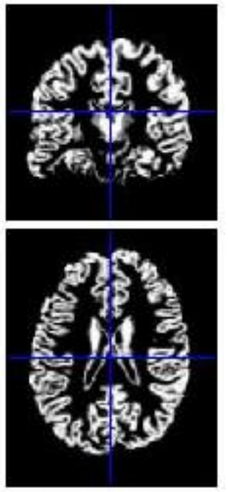

Figure 1. Example of segmented gray matter after VBM pre-processing steps.

RESULTS

Figure 2. Graphs showing the change in gray and white matter (raw volumes) over the 4 timepoints.

Cognitive Performance (Raw Scores) at 48 Months Post Injury

Participant	**Stroop Color Word**	**Digit Span**	**Trails A**(seconds)	**Trails B**(seconds)
1	111	15	12	31
2	43	11	51.3	217
3	110	18	12.8	32.5
4	111	17	19.1	51.5
5	71	17	32.97	95.07
6	112	19	18	48
7	111	19	20.6	52.7
Total Average	95.6(27.6)	16.6(2.8)	23.8(13.9)	75.4(65.9)

Table 1. Table showing raw scores for cognitive performance of each of the participants.

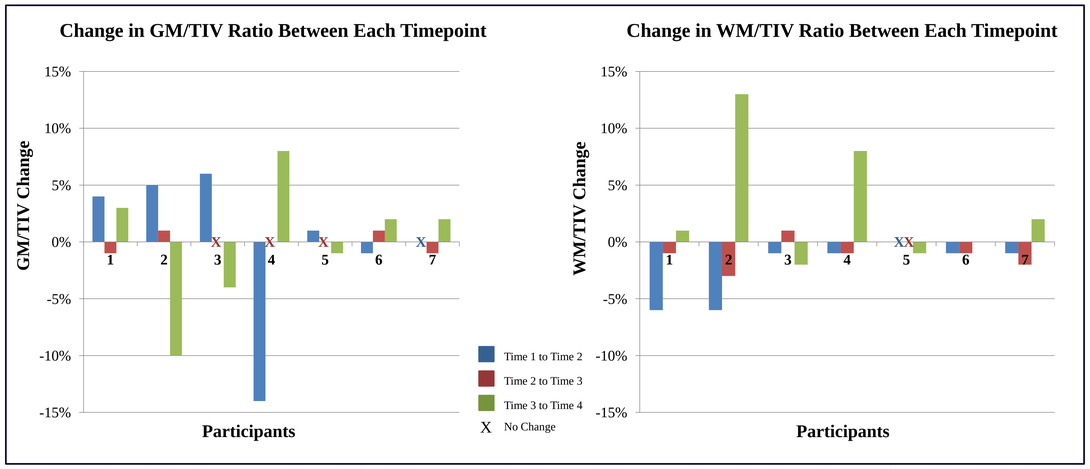

Figure 3. Graphs showing the change in brain tissue to total intracranial volume (TIV) between timepoints for each participant. Positive values mark gains in tissue volume, while negative volumes mark losses in tissue volume.

Correlations (*r*) Between Brain Tissue Volumes and Cognitive Functioning

	Stroop Task	Digit Span	Trails A	Trails B
Gray Matter/TIV				
Time 1	0.43	0.60	-0.37	-0.43
Time 2	-0.11	0.05	-0.02	0.01
Time 3	-0.18	0.00	0.06	0.09
Time 4	0.78(0.04)	0.83(0.02)	-0.85(0.02)	-0.88(0.01)
GMΔ Between Timepoints				
Time 1 & Time2	-0.33	-0.30	0.18	0.24
Time 2 & Time 3	-0.12	0.06	0.15	0.18
Time 3 & Time 4	0.79(0.04)	0.90(0.007)	-0.83(0.02)	-0.90(0.005)
Time 1 & Time 4	0.06	0.15	-0.22	-0.20
White Matter/TIV				
Time 1	-0.43	-0.60	0.37	0.43
Time 2	-0.27	-0.05	0.24	0.18
Time 3	-0.03	0.25	-0.09	-0.17
Time 4	-0.78(0.04)	-0.83(0.02)	0.85(0.02)	0.88(0.01)
WMΔ Between Timepoints				
Time 1 & Time 2	0.16	0.69	-0.10	-0.23
Time 2 & Time 3	0.49	0.55	-0.62	-0.66
Time 3 & Time 4	-0.82(0.02)	-0.76(0.05)	0.86(0.01)	0.92(0.003)
Time 1 & Time 4	-0.49	-0.06	0.53	0.49

Table 2. Table showing the correlations between performance on cognitive measures at the 4th timepoint and GM/TIV ratios, WM/TIV ratios, and the change in each tissue type over time. For significant correlations, *p*-values are shown in parentheses.

CONCLUSIONS

- The average gray and white matter volumes did not change significantly over time in our sample of participants with moderate and severe TBI.
- Significant relationships were found between performance on long term cognitive functioning and the amount of brain tissue present at the 4th timepoint, as well as with amount of change occurring in both gray and white matter between the 3rd and 4th timepoints. The results of the correlation analyses suggest that a decrease in gray matter volume and increase in white matter volume during this time is related to worse cognitive outcome.
- Individual participants varied in the amount of volumetric change over time. While not statistically significant, there was a trend for individuals with higher GCS scores to show less change than individuals with lower GCS scores.
- The findings of this study suggest that structural changes occurring *after* the first year of recovery may be crucial in predicting future cognitive outcome, having important implications for rehabilitation and intervention efforts. The negative relationship between white matter volume and cognitive performance was a surprising finding, as deficits have commonly been cited to occur with white matter loss. It is possible that there are microstructural changes which could not be detected by examining global white matter volume, that are contributing to the deficits. Future studies could benefit from using imaging techniques (such as diffusion tensor imaging) that are more sensitive to white matter integrity to better examine the relationship between structure and functioning.