

# Longitudinal diffusion tensor imaging of traumatic brain injury in a cohort of precariously housed individuals: a pre-post study with controls

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## BACKGROUND

- Marginally housed individuals frequently suffer from various comorbidities, including pervasive mental health and substance use problems.<sup>1</sup>
- They experience traumatic brain injury (TBI) at an extremely high rate, with more than half reporting a lifetime history of TBI (53.1%, 95% CI: 46.4 to 59.7%).<sup>2</sup>
- It is still unclear how TBI interacts with other health issues to impact the brain structure and function of this marginalized population, with few studies investigating the effect of TBI on their brain health.
- Here, we use diffusion tensor imaging (DTI) to investigate white matter (WM) structural changes after TBI in a cohort of marginally housed individuals and the correlation between these structural changes with symptom severity.

## HYPOTHESES

- We hypothesized that (i) compared to controls; the TBI group would show a pattern of damaged WM as suggested by the change in DTI metrics as follows: decrease in fractional anisotropy (FA), increase in mean diffusivity (MD) and radial diffusivity (RD), (ii) changes in DTI metrics would be associated with poorer clinical outcomes including higher symptom severity scores.

## METHODS

### Participants

- N=71, 37 TBI participants and 34 age-, sex-, and education-matched controls.
- Participants were recruited as part of the Hotel study, a large study investigating multimorbidity in marginalized individuals living in Downtown east side Vancouver.<sup>3</sup>
- Participants completed monthly TBI screening with TBI defined as head trauma resulting in one or more of the following: loss of consciousness, post-traumatic amnesia and/or being dazed or confused.

### DTI

- DTI uses water diffusion properties to indicate structural integrity of WM tracts, with FA, MD and RD indicating directionality, magnitude of diffusion and myelin integrity, respectively.
- Participants had baseline pre-injury DTI scans.
- Participants completed post-injury clinical assessments and DTI scans at the subacute-chronic phase at 6 weeks post-injury (range 3-12 weeks).

### Post-concussion symptom severity

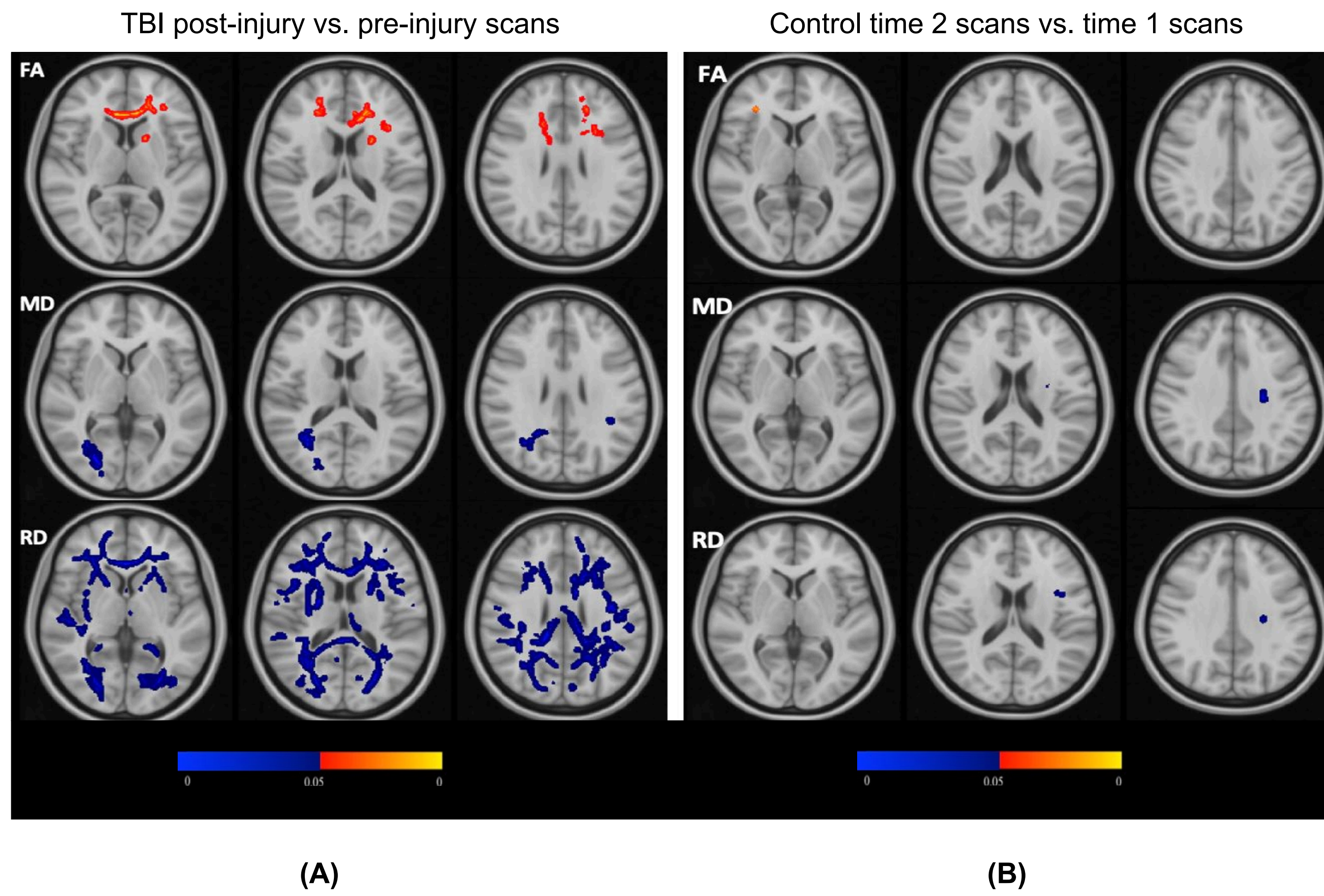
- Participants completed the Sports Concussion Assessment Tool (SCAT-3), which evaluates 22 self-reported symptoms.<sup>4</sup>
- The rating scale for symptom severity range: 0 (no symptom) - 6 (severe).
- The SCAT-3 symptom severity score range: 0-132.

### Statistical analysis

- Tract-based spatial statistics (TBSS)<sup>5</sup>: voxel-wise whole-brain analysis for FA, MD and RD were performed to analyze WM structural changes from before to after injury.
- Correlation analysis investigated the association between symptom severity scores and the longitudinal changes in DTI metrics with focus on corpus callosum (CC), given it is the WM tract commonly affected after injury.

## RESULTS

Figure1. longitudinal voxelwise analysis



(A) Longitudinal voxelwise comparison between preinjury and 6 weeks after injury in the TBI group. (B) Longitudinal voxelwise comparison between time 1 and time 2 scans in the control group. Analysis done for FA, fractional anisotropy; MD, mean diffusivity; and RD, radial diffusivity. Yellow/red indicates FA decreased postinjury relative to preinjury; blue, parameter (MD & RD) increased postinjury relative to preinjury. All results corrected for multiple comparisons using TFCE FWE at  $P \leq 0.05$ .

- Consistent with our hypothesis, voxel-wise analysis revealed a significant widespread decrease in FA, increase in MD and RD after TBI indicating loss of WM structural integrity.
- In contrast, few DTI changes were observed longitudinally in the control group (potentially indicating changes in brain structure seen with aging<sup>6</sup>), with no differences detected in white matter tracts commonly affected after injury (e.g., corpus callosum).

Figure 2. Group comparison for SCAT3 severity score showing a significantly higher score in the TBI group compared to controls ( $p=0.003$ ), indicating persistent post-TBI symptoms in the subacute/chronic phase

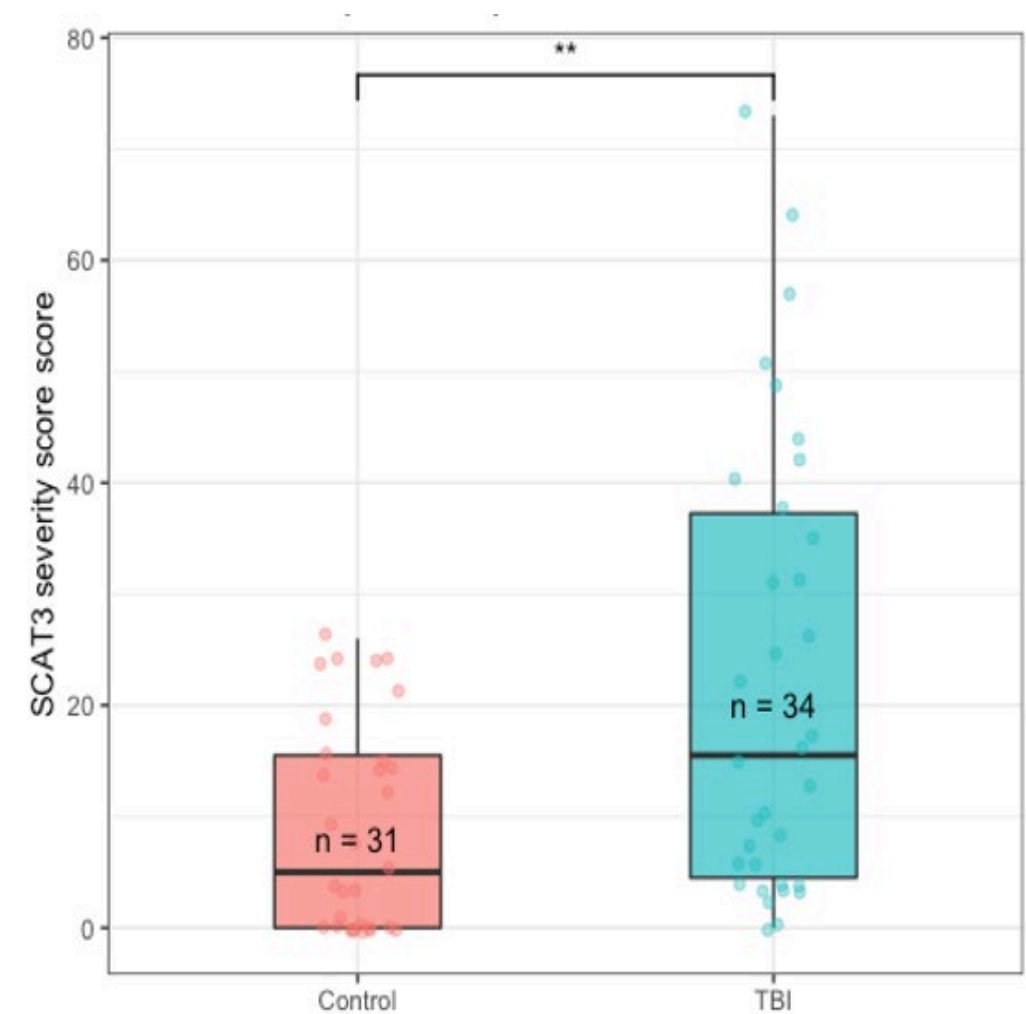
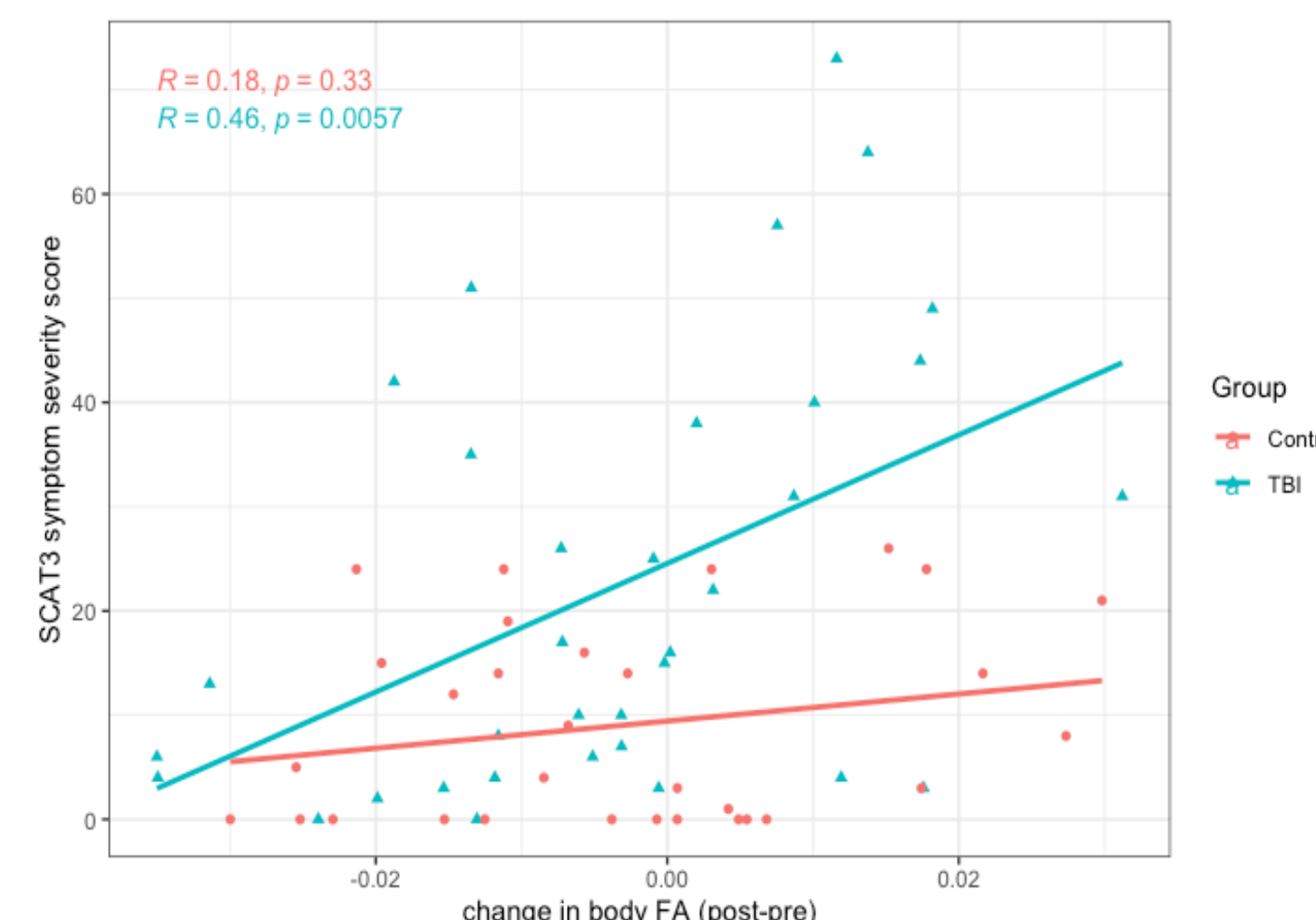


Figure 3. Correlations between SCAT3 symptom severity scores and change in the body of CC FA showing increased postinjury FA to correlate with higher severity score in TBI group ( $r=0.46$ ,  $p=0.006$ ) in contrast to our hypothesis where we expected postinjury loss of WM structure (decreased FA) to correlate with higher severity scores.



## CONCLUSIONS

- Longitudinal DTI analysis was sensitive to detecting TBI-related changes in white matter structural integrity in the subacute/chronic interval in our precariously housed group.
- The correlation between changes in CC FA and symptom severity was counterintuitive, however, few studies indicated cytotoxic edema or gliosis during the acute phase of injury as potential causes for this unexpected correlation.

## REFERENCES

1. Fazel, et al., The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. Lancet, 2014. 384(9953): p. 1529-40.
2. Stubbs, J.L., et al., Traumatic brain injury in homeless and marginally housed individuals: a systematic review and meta-analysis. The Lancet Public Health, 2020. 5(1): p. e19-e32.
3. O'Connor, T.A., et al., Traumatic brain injury in precariously housed persons: Incidence and risks. EClinicalMedicine, 2022. 44: p. 101277.
4. Guskiewicz, K.M., et al., Evidence-based approach to revising the SCAT2: introducing the SCAT3. Br J Sports Med, 2013. 47(5): p. 289-93.
5. Smith, S.M., et al., Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. Neuroimage, 2006. 31(4): p. 1487-505.
6. Bender, A.R., et al., Differential aging of cerebral white matter in middle-aged and older adults: A seven-year follow-up. Neuroimage, 2016. 125: p. 74-83.



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