

# Changes in alcohol consumption post-trauma are significantly associated with reward—related brain activation



Hinojosa, C.A., Ph.D.<sup>1</sup>, van Rooij, S.J.H., Ph.D.<sup>1</sup>, Harnett, N.G. Ph.D.<sup>2,3</sup>, Lebois, L.A.M.<sup>2,3</sup>, Ph.D., Murty, V.P., Ph.D.<sup>4</sup>, Jovanovic, T., Ph.D.<sup>5</sup>, House, S., M.D., Ph.D.<sup>6</sup>, Fani, N., Ph.D.<sup>1</sup>, McLean, S.A., M.D., M.P.H.<sup>7,8</sup>, Ressler, K.J., M.D.<sup>2,3</sup>, Ph.D., & Stevens, J., Ph.D.<sup>1</sup>

<sup>1</sup>Department of Psychiatry & Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA; <sup>2</sup>Division of Depression and Anxiety, McLean Hospital, Belmont, MA, USA; <sup>3</sup>Department of Psychiatry, Harvard Medical School, Boston, MA, USA; <sup>4</sup>Department of Psychology, Temple University, Philadelphia, PA, USA; <sup>5</sup>Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA; <sup>6</sup>Department of Emergency Medicine, Washington University School of Medicine, St. Louis, MO, USA; <sup>7</sup>Institute of Trauma Recovery, Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>8</sup>Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

## Grady Trauma Project

## Background

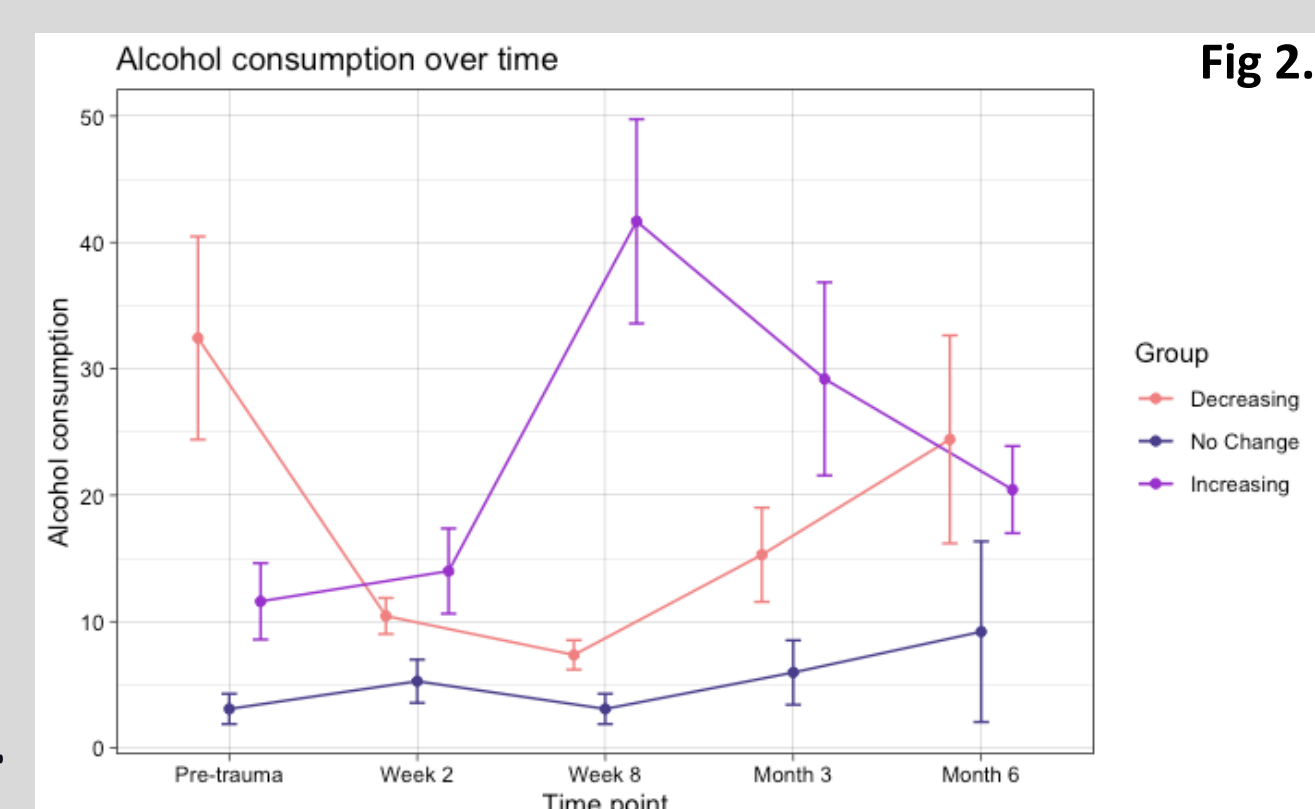
- Posttraumatic stress disorder (PTSD) and problematic alcohol use frequently co-occur,<sup>1</sup> and the neural factors that contribute to the development of problematic alcohol use after acute trauma exposure are unknown.
- Using a multi-site longitudinal study design, we explored whether the change in alcohol consumption pre-trauma to 8 weeks post-trauma was associated with reward-related brain reactivity and functional connectivity (FC) measures gathered 2-weeks post-trauma.
- Exploring reward-related brain alterations in PTSD is important to potentially uncover the underlying mechanisms promoting alcohol use.

## Research Question

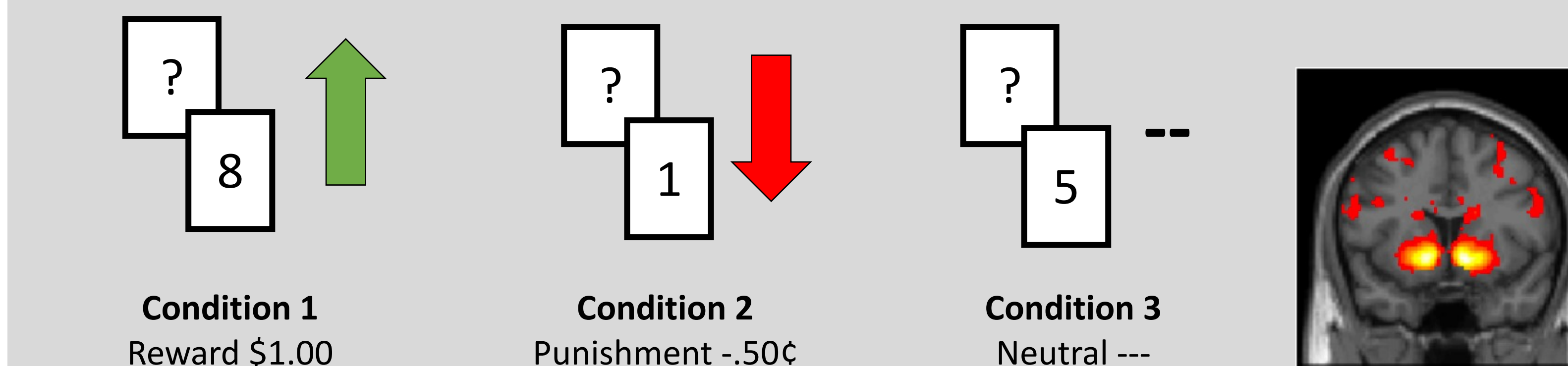
- Explore associations between alcohol change scores (pre-trauma to 8 weeks post-trauma) and reward-related reactivity and functional connectivity (2-weeks post-trauma).
- Determine whether significant differences in brain measures exist between three alcohol change groups: those who increased use, decreased use, or showed now change in alcohol use.

## Methods

- Participants were recruited from emergency departments across the U.S. as part of the AURORA study (N=286; n=178 Female).
- Alcohol consumption (drinks per month; PhenX Toolkit<sup>2</sup>) was assessed for the month prior to the trauma and again 8 weeks post-trauma.
- Trauma-related change in drinking was quantified as the change in 30-day total drinking at 8 weeks, relative to pre-trauma.
- Reward-related neural reactivity was assessed at 2 weeks post-trauma using functional magnetic resonance imaging (fMRI) during a monetary reward task (**Fig. 1**) and analyzed in *fMRIprep* and *SPM12*. Structural regions of interests (ROIs) were extracted using the Reinforcement Learning Atlas.<sup>3</sup> *R* (v4.2.1) was used to conduct statistical analyses.
- Seed-based FC analyses examining the association between reward-related reactivity and change in alcohol consumption were conducted using *CONN Toolbox* (v21.a).
- Reward-related neural reactivity was compared across those whose alcohol consumption increased (n=99, n=60 Female), decreased (n=103, n=67 Female), or did not change (n=84, n=51 Female), (**Fig. 2**).



## Monetary Reward Task



**Fig. 1.** Overview of the modified monetary reward task from Delgado et al., 2000<sup>4</sup>

## Results

### Correlational Analyses

**Table 1.** Correlation Matrix Across Alcohol Change Scores and Reward-related Reactivity (Gain > Loss)

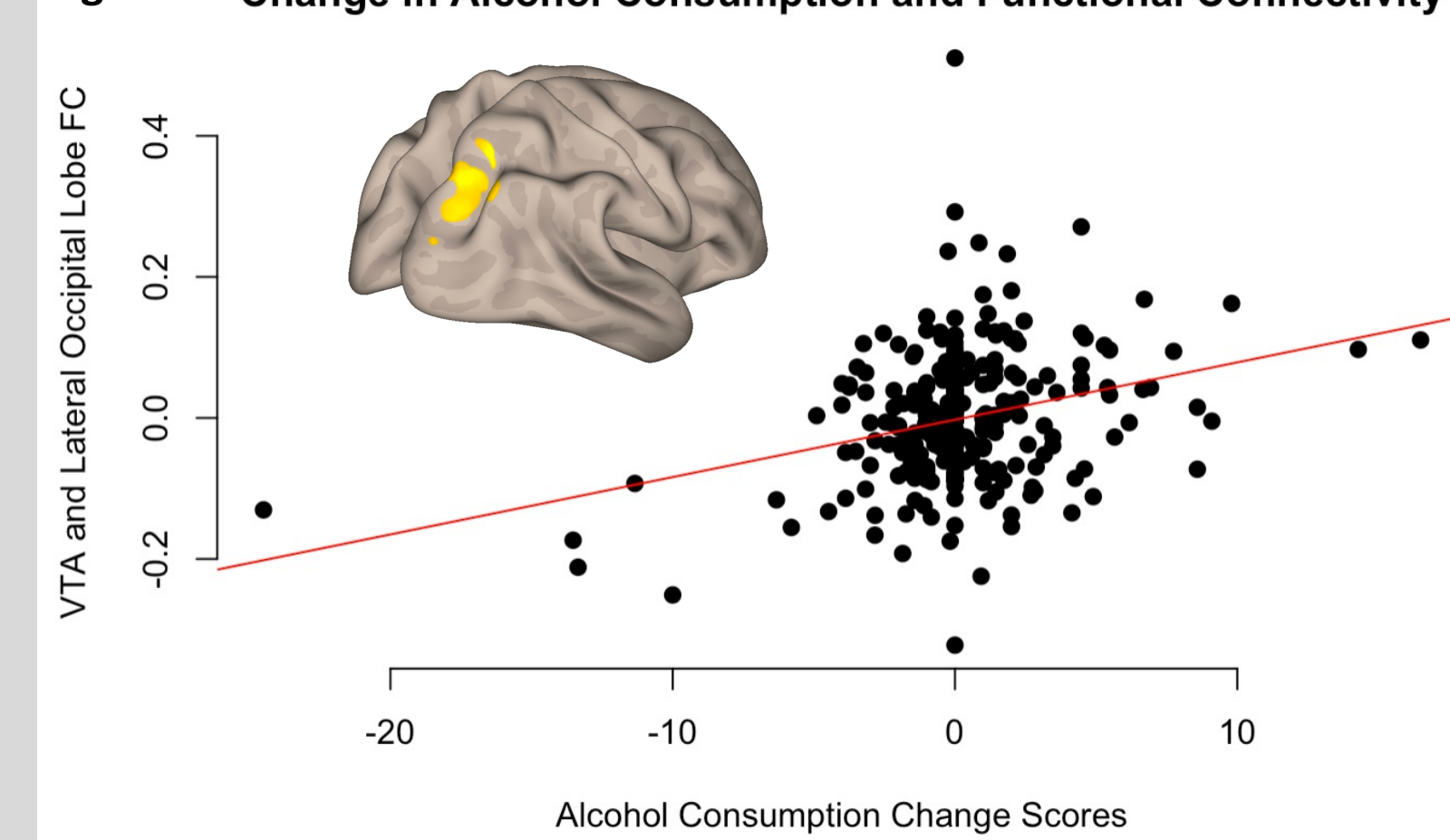
Variable	Mean (SD)	1	2	3	4	5	6	7
1. Alcohol Consumption Change Scores	.17 (3.38)	-						
2. VTA	-.02 (.64)	.22**	-					
3. Nucleus Accumbens	.56 (.62)	.12	.20**	-				
4. Globus Pallidus External	.05 (.35)	.07	.19**	.05	-			
5. Globus Pallidus Internal	-.02 (.37)	.01	.17**	.03	.54**	-		
6. Caudate	.17 (.41)	.02	.22**	.42**	.36**	.12*	-	
7. Putamen	.16 (.36)	.03	.13*	.34**	.49**	.21**	.59**	-

Note. Abbreviations: VTA = ventral tegmental area.  
\*\* $p < .001$ , \* $p < .05$

A significant positive correlation was found between VTA reactivity to the Gain > Loss contrast and change scores in alcohol consumption.

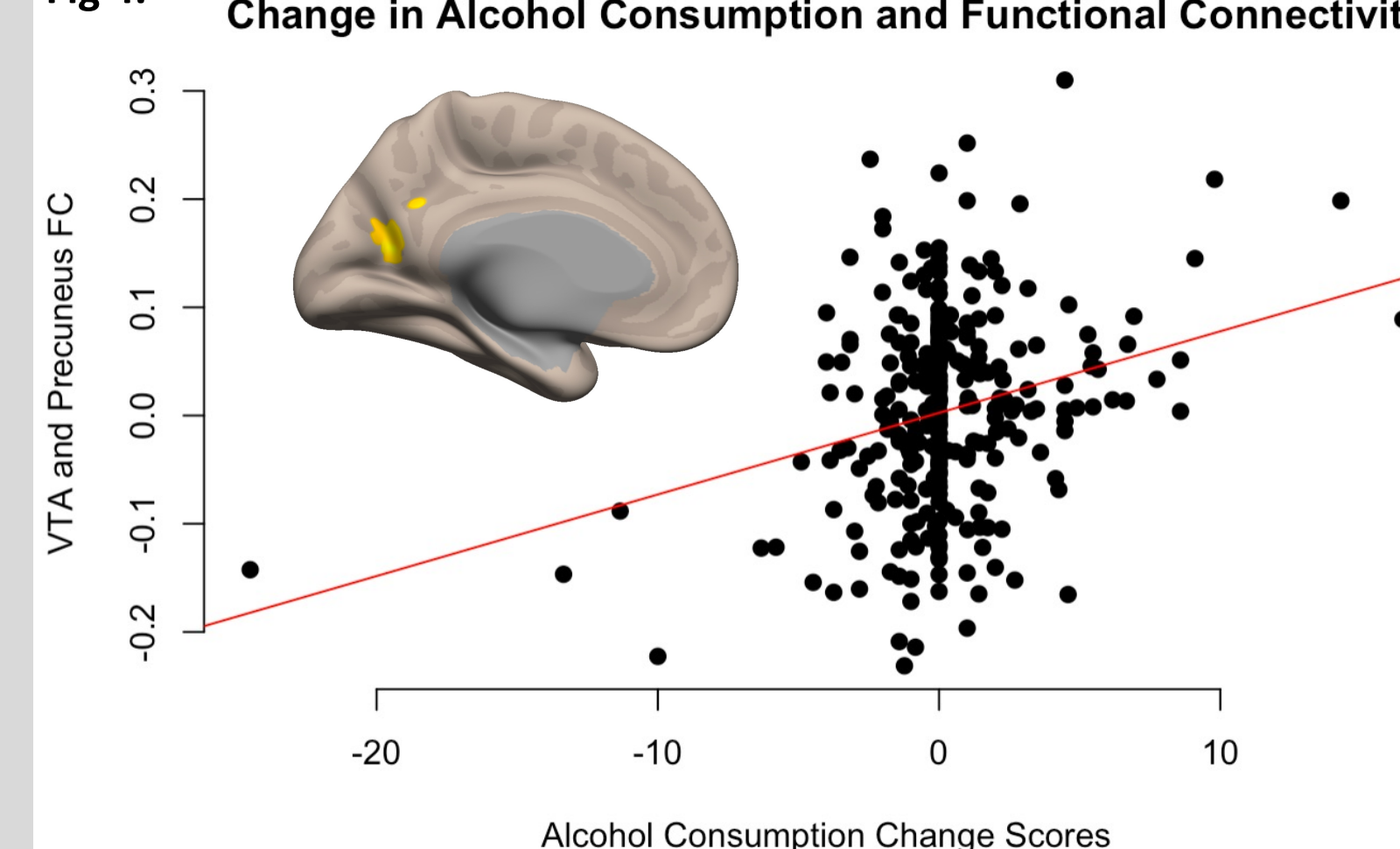
### Functional Connectivity Analyses

**Fig 3.** Change in Alcohol Consumption and Functional Connectivity



Greater FC between the VTA seed and lateral occipital cortex (MNI, x=28, y=-76, z=50) was associated with greater change in alcohol consumption, cluster-level  $P_{FWE} < .001$ ,  $K_E = 607$ , (**Fig. 3**).

**Fig 4.** Change in Alcohol Consumption and Functional Connectivity

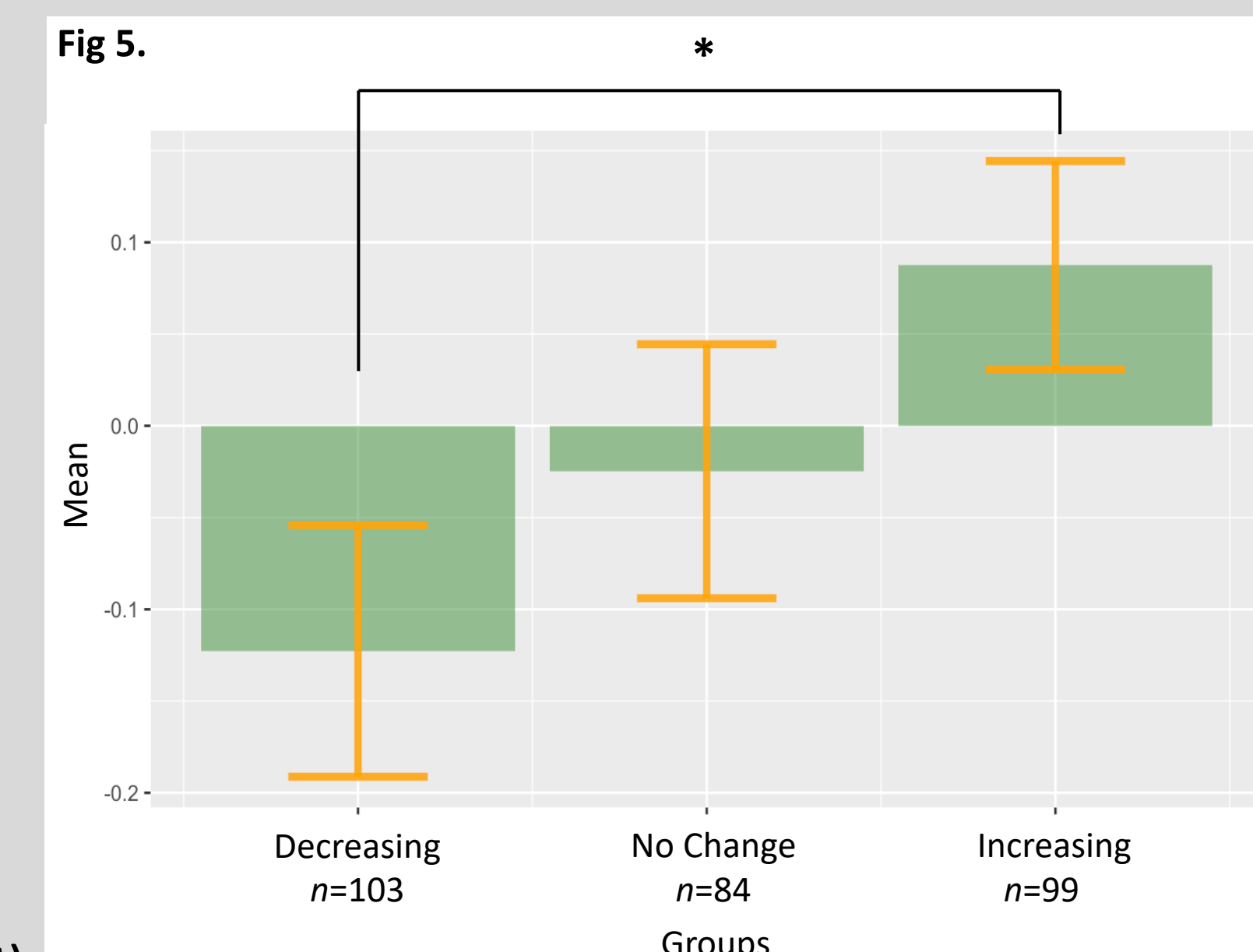


Greater FC between the VTA seed and the precuneus (MNI, x=-20, y=-60, z=18) was associated with greater change in alcohol consumption, cluster-level  $P_{FWE} = 0.014$ ,  $K_E = 290$ , (**Fig. 4**).

## Results

### Group Differences

Analysis of variance (ANOVA) exhibited a significant group difference,  $F(1, 284) = 5.56$ ,  $p = 0.02$ . The increasing alcohol consumption group exhibited greater VTA activation ( $M = .09$ ,  $SD = .56$ ) than the decreasing alcohol consumption group ( $M = -0.12$ ,  $SD = .70$ ; **Fig. 5**).



## Implications

- Clarifying the relationship between PTSD symptoms and alcohol use will lead to intervention development for those recently exposed to trauma.
- The findings presented provide evidence that changes in alcohol consumption early post-trauma may contribute to reward alterations in trauma-exposed individuals.
- Uncovering the neural correlates of alcohol use in recently trauma-exposed participants is pivotal in determining who would benefit most from early interventions to prevent the development of trauma-related psychopathology.

## Future Directions

- These findings align with previous research that suggest an initial increase in reward-related brain activation may contribute to the reinforcing effects of substances contributing to increased use of the substance, potentially leading to dependence.
- Latent class analysis can be used to determine different longitudinal trajectories of alcohol use after trauma exposure and whether significant differences exist between these classes in reward-related neurocircuitry.

### References

- Pietrzak, R.H., Goldstein, R.B., Southwick, S.M., & Grant, B.G. (2011). Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Anxiety Disorders*, 25, 456-465.
- Hamilton, C.M., Strader, L.C., Pratt, J.G., et al. (2011). The PhenX Toolkit: get the most from your measures. *Am J Epidemiol*, 174(3), 253-260.
- Pauli, W., Nili, A., & Tyszka, J. (2018). A high-resolution probabilistic in vivo atlas of human subcortical brain nuclei. *Sci Data*, 5, 180063.
- Delgado, M.R., Nystrom, L.E., Fissell, C., Noll, D.C., & Fiez, J.A. (2000). Tracking the hemodynamic responses to reward and punishment in the striatum. *J Neurophysiol*, 84(6), 3072-3077.

