

Variations in caudate and hippocampus volume and shape during response and spatial learning

Victor R. Schinazi[∞], Tyler Thrash[∞], Ruth O’Gorman Tuura[§], Christoph Hölscher[∞] and Gregor Hasler⁺

[∞]Chair of Cognitive Science, ETH Zürich; [§]Center for MR-Research, University Children’s Hospital Zürich, ⁺University Hospital of Psychiatry, University of Bern

1. Introduction

The contributions of the hippocampus and caudate to spatial and response learning have been dissociated in terms of the relationships between selective chemical lesions and path choice in rats⁸, neural activation and self-reported strategy⁵, grey matter volume and spontaneous strategy¹, and grey matter volume and judgments of relative direction⁹. While differences in regional (i.e., global) volumes are useful for dissociating these two regions during navigation, shape analysis may be more sensitive to local variations^{6,7}. This fine-grained approach can further constrain theories of response and spatial learning by identifying subregions responsible for the performance of specific tasks. In the present study, we investigated global and local differences in the volumes of the caudate and hippocampus associated with response and spatial tasks, respectively.

2. Method

24 participants

- 4 excluded (simulator sickness)
- 10 women and 10 men analyzed (mean age = 25; range = 19 to 38)

Procedure (x5 blocks)

- Joystick training
- 5 training trials with navigation aid (i.e., arrow or map)
- 1 testing trial without navigation aid

Analysis

- Behavioral analysis – trial x task design
- Volumetric analysis – hippocampus and caudate only
- Shape analysis – local differences in growth and atrophy

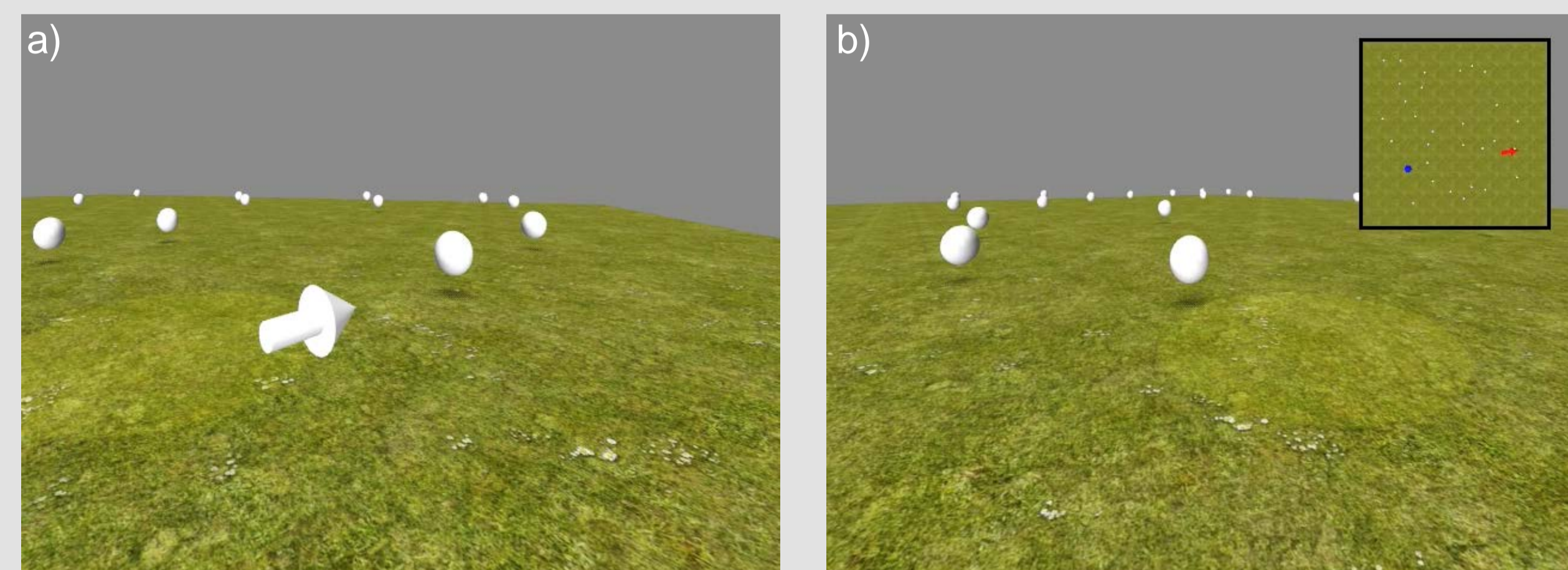
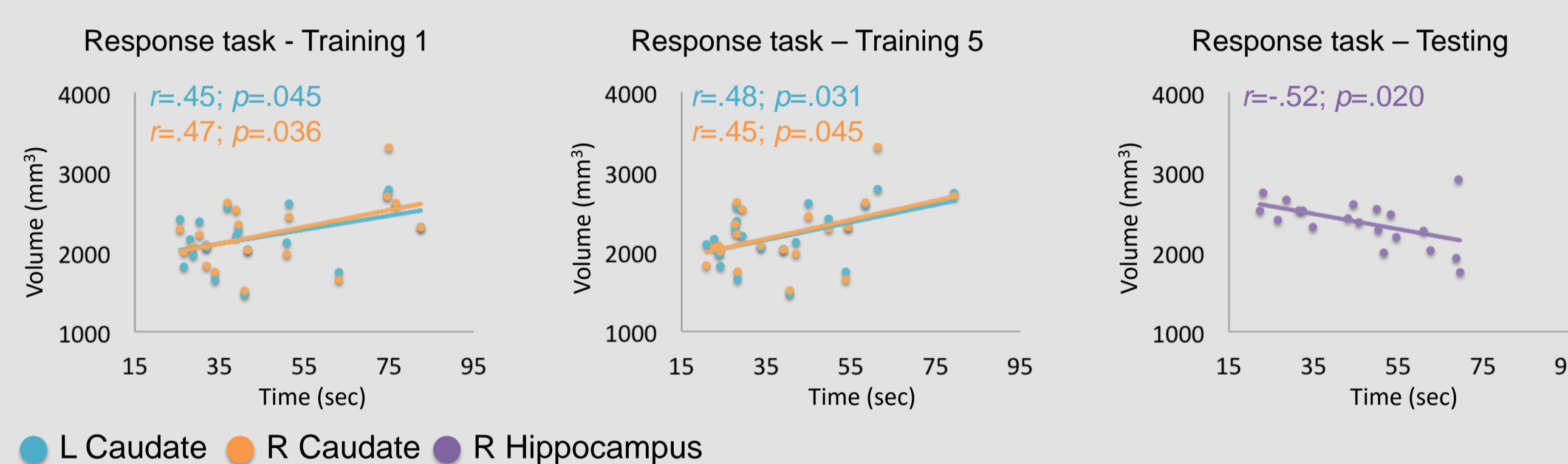


Figure 1. Screenshots for (a) response and (b) spatial tasks. For the response task, participants were instructed to follow the direction indicated by an arrow along an elliptical path. For the spatial task, participants were instructed to move from their starting location to the goal location as efficiently as possible. The red arrow on the map represented the starting location and orientation, and the blue circle represented the goal location. Neither location was indicated from a first-person perspective.

3. Results volume and shape

Volumetric analysis

Hippocampal and caudal volumes for each participant were determined using cortical reconstruction and volumetric segmentation of T1 structural images (FreeSurfer⁴). Subcortical regions were normalized to the estimated total intracranial volume (eTIV) using an analysis of covariance approach². These regional volumes were correlated with the time required to complete the first training trial, the fifth training trial, and the testing trial. Voxel-based morphometry (VBM) was also used to test for volume differences. Notably, the VBM results did not survive correction for multiple comparisons.



● L Caudate ● R Caudate ● R Hippocampus

Figure 2. Volumetry results. (a) Positive correlations were found between the time required to complete the first training trial (aggregated over block) for the response task and the volumes of both the right and left caudate. (b) Positive correlations were found between the time required to complete the final training trial (aggregated over block) for the response task and the volumes of both the right and left caudate. (c) A negative correlation was found between the time required to complete the testing trial (aggregated over block) for the response task and the volume of the right hippocampus.

Shape analysis

Shape analysis was conducted using FSL FIRST³. We used a single regressor model specifying the predicted relationship between task performance (e.g., response task – training 1) and growth or atrophy at individual vertices on hippocampal and caudal surfaces.

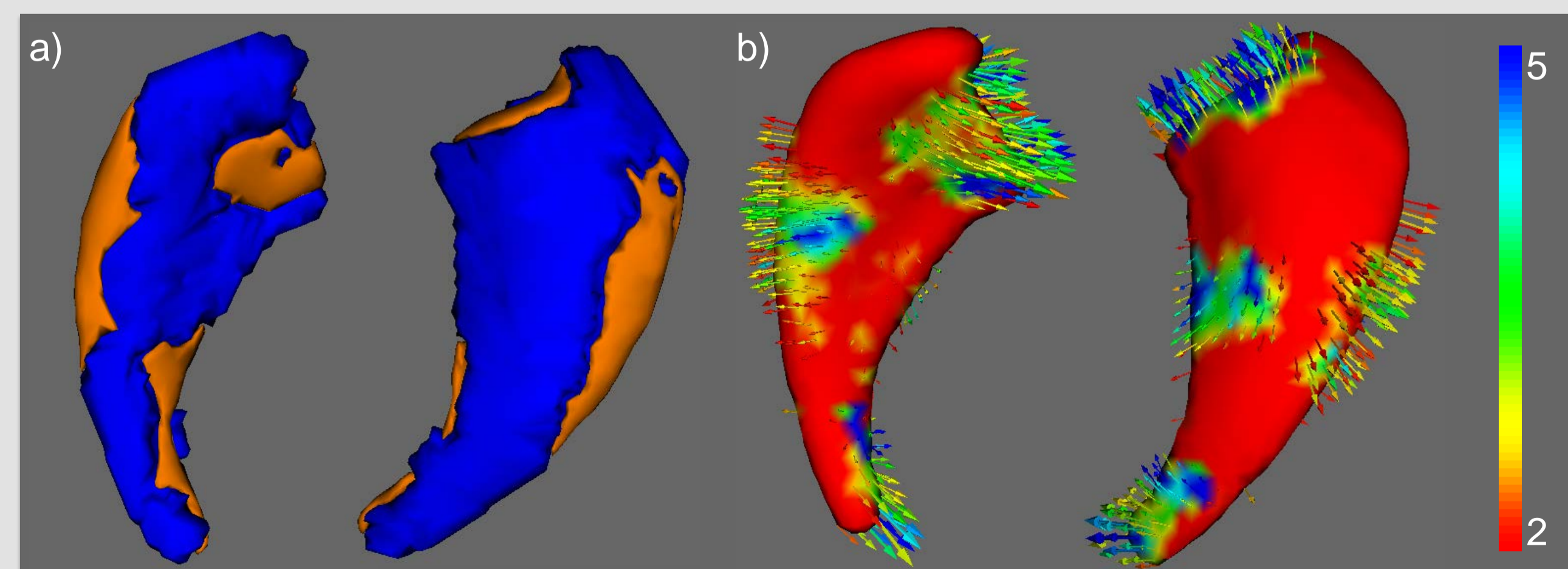


Figure 3. Shape analysis results. (a) Areas of significant change (orange) for the right caudate in relation to response task performance for the first training trial, $p = .05$ (uncorrected). (b) Direction and strength of shape changes for the right caudate. Arrows indicate the direction of change (i.e., growth or atrophy), and the color of the vertices correspond to the size of the F statistic, $p = .05$ (uncorrected). These patterns of growth indicate specific subregions of the head, body, and tail of the right caudate related to early task performance. No other significant effects were found in the caudate or hippocampus.

4. Results behavioral

We conducted a 3 (trial) x 2 (task) ANOVA omitting training trials 2 through 4. We found a significant two-way interaction, $F_{(2,38)}=39.104$, $MSE=297.807$, $p<.0001$. Participants performed faster on the first training trial for the response task than for the spatial task. However, participants performed faster on training trial 5 and testing for the spatial task than the response task.

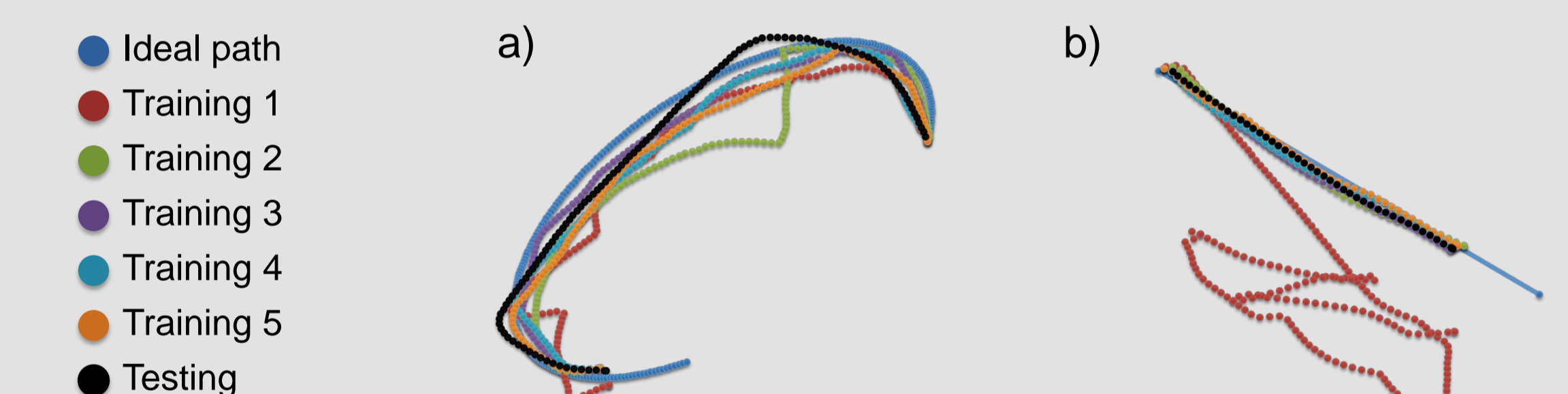
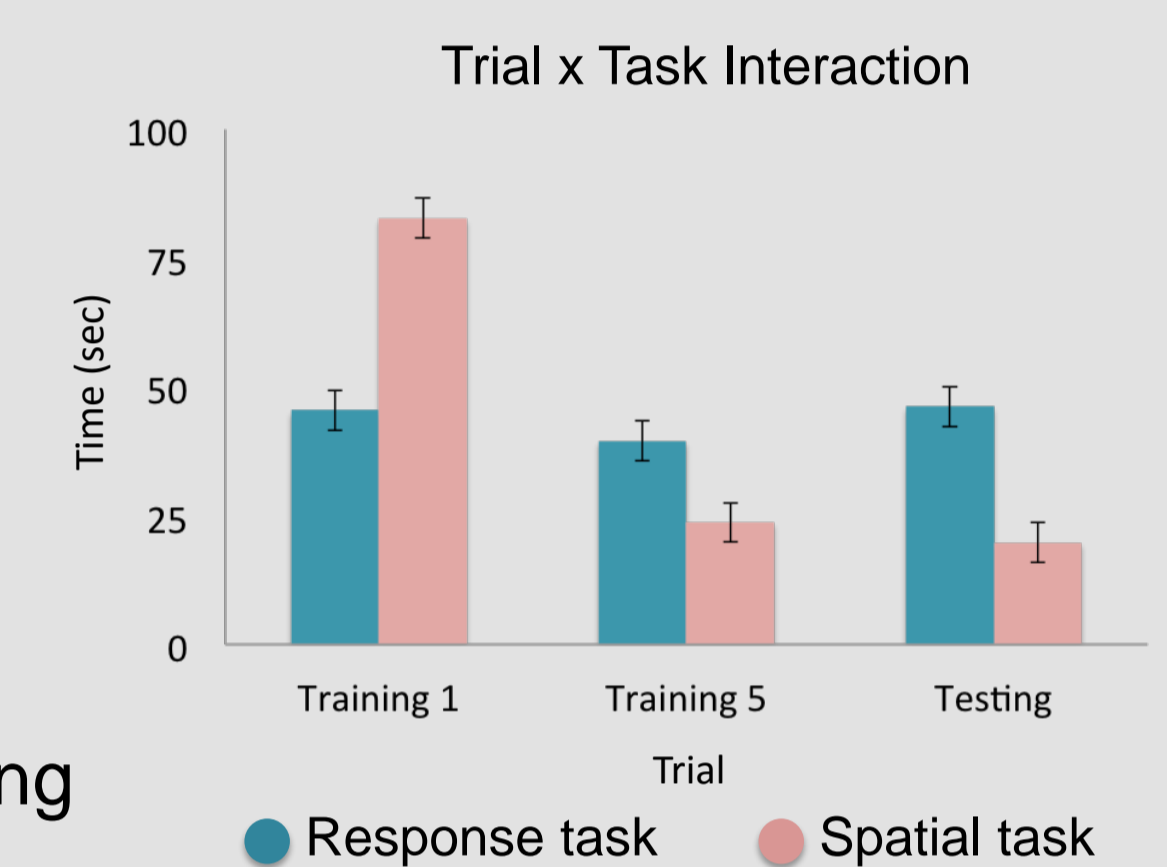


Figure 4. Examples of paths from one block and one participant of the (a) response and (b) spatial tasks.

5. Conclusion

Behavioral results indicate differences in the learning profiles of participants with respect to response and spatial tasks. Volumetric analysis revealed different patterns of caudal and hippocampal involvement associated with the response task but not the spatial task. When the compass was present, the volume of caudate (bilaterally) positively correlated with time required to complete the response task. When the compass was absent, the volume of the right hippocampus negatively correlated with time required to complete the response task. Shape analysis revealed growth at specific locations in the right caudate related to performance on the first training trial of the response task. Together, these findings suggest that the participants adopted a spatial strategy for the response task. Local differences in the right caudate may underlie this strategy.

6. References

1. Bohbot, V. D., Lerch, J., Thordarson, B., Iaria, G., & Zijdenbos, A. P. (2007). Gray matter differences correlate with spontaneous strategies in a human virtual navigation task. *J Neurosci*, 27(38), 10078–83.
2. Free S, Bergin P, Fish D, Cook M, Shorvon S, Stevens J. Methods for normalization of hippocampal volumes measured with MR. *AJNR Am J Neuroradiol*. 1995;16:637–643.
3. <http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIRST>
4. <http://surfer.nmr.mgh.harvard.edu>
5. Iaria, G., Petrides, M., Dagher, A., Pike, B., & Bohbot, V. D. (2003). Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *J Neurosci*, 23(13), 5945–52.
6. Levitt, J. J., Westin, C. F., Nestor, P. G., Estepar, R. S. J., Dickey, C. C., Voglmaier, M. M., ... Shenton, M. E. (2004). Shape of caudate nucleus and its cognitive correlates in neuroleptic-naïve schizotypal personality disorder. *Biological Psychiatry*, 55(2), 177–84.
7. McHugh, T. L., Saykin, A. J., Wishart, H. A., Flashman, L. A., Cleavinger, H. B., Rabin, L. A., ... Shen, L. (2007). Hippocampal volume and shape analysis in an older adult population. *The Clinical Neuropsychologist*, 21(1), 130–45.
8. Packard, M. G., & McGaugh, J. L. (1996). Inactivation of Hippocampus or Caudate Nucleus with Lidocaine Differentially Affects Expression of Place and Response Learning. *Neurobiology of Learning and Memory*, 65(1), 65–72.
9. Schinazi, V. R., Nardi, D., Newcombe, N. S., Shipley, T. F., & Epstein, R. A. (2013). Hippocampal size predicts rapid learning of a cognitive map in humans. *Hippocampus*, 23(6), 515–528.