

Hemispheric asymmetry in the hippocampus of birds assessed with rsfMRI

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Introduction: Both brain hemispheres exhibit strong, but not complete, bilateral symmetry in both structure and function. Nevertheless some brain functions are lateralized with the most evident example the phenomena of right- or left-handedness. Moreover atypical lateralization in brain structure and function is associated with neuropsychiatric disorders such as autism spectrum disorders and schizophrenia¹. Earlier we have shown the usefulness of rsfMRI to study lateralization in the brain by applying this technique to a well-known model of lateralization, the visual system of the awake pigeon². In this study we wanted to extend this application to another avian brain region, the hippocampus, of which a large body of data has accumulated demonstrating its functional lateralization. In this study the protocol was applied to two species.

Methods: In this study, 11 European starlings (*Sturnus vulgaris*) were used. Resting state fMRI scans were acquired for all birds anesthetized with 1% isoflurane (IsoFlo, Abott, Illinois, USA) administered in a mixture of 30% O₂ and 70% N₂. Moreover, 8 pigeons (*Columba livia*) of the Valentia Figurita breed were measured after they were trained to be scanned while awake following the protocol of De Groof & Jonckers et al.². The resting state fMRI data were recorded using a 7T Biospec scanner (Bruker, Ettlingen, Germany) using a RAREst sequence with a repetition time (TR) of 2000ms, and echo times (TE) of 15 and 16 ms. Voxel size was 0.18/0.17 x 0.36/0.34 mm². 14 axial slices with a slice thickness of 0.7/0.8mm were recorded. 150 repetitions of each image were acquired, resulting in a measuring time of approximately 5 minutes per sequence. Standard pre-processing was carried out using the Statistical Parametric Mapping 8 program (SPM 8) (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8>)². REST time courses were extracted for four seed regions, which were located in left and right anterior hippocampus, and left and right posterior hippocampus (figure 1). Functional connectivity (FC) maps were generated in SPM⁸. Both motion parameters, resulting from the realignment, as well as global signal time courses were regressed out during this analysis to improve the specificity of the FC⁴.

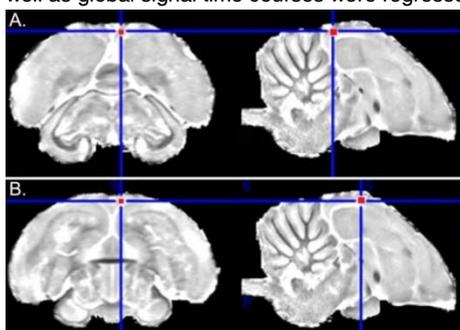


Figure 1 Posterior (A) and anterior (B) seed location overlaid on an anatomical MRI image of the starling brain.

Discussion and Conclusion: The outcome of this study shows a lateralization in hippocampal FC in starling and in pigeon. Both in awake and anesthetized animals, the same conclusion could be reached, reinforcing the validity of the results. The left sided larger cluster size points to a larger neural network that can be recruited by structures that are functionally dominant for tasks like spatial navigation. This study clearly shows the possibility to study lateralization of brain functioning with rsfMRI which opens future opportunities at both the preclinical as well as clinical level extending the existing knowledge on functional brain lateralization⁵.

Results: Cluster sizes were calculated for all seeds for all starlings and compared between hemispheres. This revealed a significantly larger cluster size in the left hemisphere compared to the right hemisphere both for the posterior seed location ($p=0.013$) as for the anterior seed location ($p=0.037$). Nevertheless, the difference was more distinct for the posterior seed location (figure 2). Similar FC data were acquired in the 8 awake pigeons (6 datasets each). Seed regions were selected to be as similar as possible to the regions used in the starlings. Similar to the starling outcome, the anterior hippocampal seed showed a significant higher local FC in left hippocampus compared to right hippocampus ($p=0.022$). Moreover a similar trend towards higher FC in the left hemisphere was seen for the posterior seed ($p=0.052$).

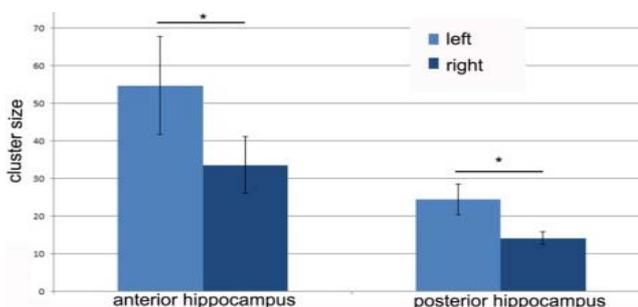


Figure 2: Mean cluster sizes (+/- SEM) in left and right hippocampus for the anterior and posterior hippocampal seed regions from all starlings.

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