Dentate gyrus geometry shapes hippocampal circuitry

Memory formation involves sequential sensory information processing in several brain subregions with intricate circuitries such as dentate gyrus (DG) and CA3. How these circuits are connected via the principal cell types, namely granule and pyramidal cells, affects the computations performed on the sensory information flow. Some studies suggest that this connectivity is mainly determined by the ratio of these principal cell types along different anatomical axes. In turn, these ratios are mainly determined by the geometry of the involved structures. To see how the geometry affects the connectivity between these circuitries, we have developed a 3D model of the dentate gyrus and CA3 areas. Furthermore, we investigate the effect of increased globularity (due to brachycephaly) which has been shown to highly influence neuronal network connectivity in the context of Down syndrome (DS).

We investigated how 3D geometry influences cell distribution in the DG along the septotemporal axis, numbers of different neuronal subtypes were extracted from the Hippocampome database, and neurons were randomly distributed using Poisson disc distribution. Neurons within sublayers were randomly assigned to various subtypes.

Upon cell distribution, in-silico slicing was made along the septotemporal axis to compare cell densities with previously published experimental data. Similar analyses were done on the DS brain using MRI data. The results of our study surprisingly revealed that despite randomly distributing the cells in the DG 3D geometry, cell ratios along the septotemporal axis of the DG and CA3 closely matched experimental data. This finding suggests that the 3D geometry of the DG influences its anatomical properties.

In conclusion, our study provides compelling evidence that the 3D geometry of the DG may play a role in shaping cell distribution ratios, and provides a unique tool to explore how brain morphology affects topological properties, neural connectivity, and function. It also opens the possibility of studying disorders involving morphological changes affecting the hippocampal shape, such as Down syndrome, or William Beuren syndrome.