Integrating MR with 3D Gene Expression Data in the Mouse Brain

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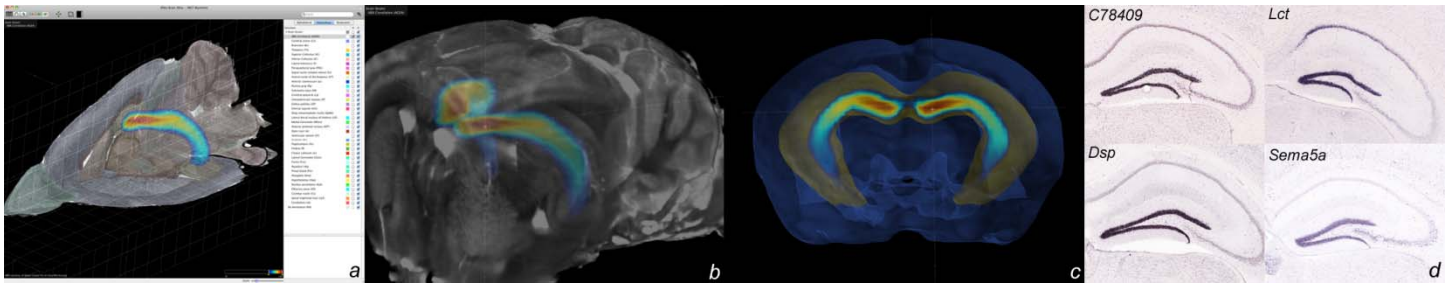
Introduction

The Allen Brain Atlas (ABA) is a database of over 20,000 *in situ* gene expression patterns in the adult C56BL/6J mouse brain mapped into a common coordinate system [1]. We registered the ABA reference volume (reconstructed from Nissl stained histological images at 25 μm^3 resolution) to a set of multispectral MR volumes (T1, T2, and T2*) at 21.5 μm^3 resolution [2]. This set of MR volumes defines a coordinate representation standard called Waxholm space and is freely available to allow interoperation between disparate mouse brain imaging resources [3]. A viewer was developed to co-visualize ABA gene expression and MR data and also query the ABA online database at regions of interest in the MR space. This tool provides an interactive, direct, and easy-to-use link between MR studies and a widely-used database of gene expression patterns.

Methods

The ABA was registered with Waxholm space by maximizing the mutual information of manually annotated brain regions in each 3d space. The deformation was parameterized with a multiscale 3d B-spline grid. The ABA's 3d desktop visualization application, Brain Explorer, was adapted for use with MR images and to transform data between Waxholm and ABA space. Brain Explorer was also updated with hardware-accelerated volume rendering engine running on commodity 3d graphics hardware.

Results



(a) shows the full resolution Waxholm T1 MR image sliced on orthogonal planes. The color overlay on the planes indicates a segmentation of 37 anatomic regions from the MR image [2]. The blue-orange-yellow overlay is an ABA gene expression correlation map (AGEA: http://mouse.brain-map.org/agea) rendered by maximum intensity projection. The correlation maps show voxels where gene expression is highly correlated with a seed voxel—in this example, the dentate gyrus as defined by gene expression is shown. The seed voxel was chosen in Waxholm space by navigating the T1 MR image in which the hippocampus is clearly visible. The coordinates were transformed to ABA space, the corresponding correlation volume requested from the ABA web service, and the returned volume transformed back to Waxholm space for viewing. **(b)** shows the correlation volume in (**a)** merged with a volume rendering of the T1 image clipped to a region of interest around the hippocampus. **(c)** adds a surface representation of the hippocampus segmentation [2] in yellow and cortex in blue to show the gene expression-defined dentate gyrus in relation to an MR anatomy-defined hippocampus. The correlation map in **(a-c)** was used to find similar gene expression patterns using the AGEA gene finder web service, and the top 4 results are shown in **(d)**.

Discussion

The results above illustrate a workflow from MR data to a database of high resolution *in situ* gene expression patterns. If MR studies are registered to the Waxholm MR target volumes, lists of genes with expression in regions of interest from the MR data can now be readily queried for further analysis and investigation. The utility of these tools is expected to increase as more mouse brain imaging resources are registered with Waxholm space.

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