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Structural connectivity of the Parkinson's disease mouse model basal ganglia: Diffusion MRI Tractography study

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Parkinson's disease (PD) is one of the most common neurological disorders and is a degenerative neuropathy that affects both motor function and cognition. Studies of Basal ganglia neuronal connectivity in Parkinson's disease (PD) using MRI have shown promising results but remains incomplete. This study provides a comprehensive analysis of PD-related changes in mouse basal ganglia neuronal connectivity between control group and disease group by comparing tractography generated from each basal ganglia structure. Experiments were performed in four month old female mice (control: TetP-AIMP2 (n=2) and disease: 3X-Tg (n=2)). Mouse transcardially were perfused and fixed with 4% paraformaldehyde and 0.1% Magnevist® in phosphate buffer (PB). Brains were extracted and incubated in 0.1% Magnevist/phosphate buffer for 4 days, placed in Fomblin and imaged. Image acquisition was conducted on a 9.4 T Bruker BioSpec horizontal bore, dedicated animal scanner (Bruker Biospin, Ettlingen, Germany). The pulse sequence used for this acquisition was 3D TurboRARE T2 and 2D EPI-Diffusion tensor. In this study, we were able to use the Allen Mouse Brain Atlas for the accurate segmentation of the basal ganglia, then use the segmentations for generating neuronal connectivity of basal ganglia structures in PD mice using high resolution 9.4T MRI. Quantitative analysis of the basal ganglia shows decrease in FA and increase in MD, which were found to be in part consistent with previous studies on Parkinson's disease. In addition, the connectivity matrix results show that the Parkinson group had a smaller overall signal intensity range than the control group, and that the mouse basal ganglia's interconnectivity is almost consistent with previous studies on human basal ganglia interconnectivity. We were able to visualize the neural connectivity of Parkinson's disease-related biomarkers in the control and disease groups, and observe the reconstruction of connectivity between the structures.

Key Words: Tractography, Parkinson's disease, Basal ganglia, Diffusion tensor image, Mouse

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Effect of diverse recoding of granule cells on optokinetic response in a cerebellar ring network with synaptic plasticity

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We consider a cerebellar ring network for the optokinetic response (OKR), and investigate the effect of diverse recoding of granule (GR) cells on OKR by varying the connection probability pc from Golgi to GR cells. For an optimal value of pc* (=0.06), individual GR cells exhibit diverse spiking patterns which are in-phase, anti-phase, or complex out-of-phase with respect to their population-averaged firing activity. Then, these diversely-recoded signals via parallel fibers (PFs) from GR cells are effectively depressed by the error-teaching signals via climbing fibers from the inferior olive which are also in-phase ones. Synaptic weights at in-phase PF-Purkinje cell (PC) synapses of active GR cells are strongly depressed via strong long-term depression (LTD), while those at anti-phase and complex out-of-phase PF-PC synapses are weakly depressed through weak LTD. This kind of "effective" depression (i.e., strong/weak LTD) at the PF-PC synapses causes a big modulation in firings of PCs, which then exert effective inhibitory coordination on the vestibular nucleus (VN) neuron (which evokes OKR). For the firing of the VN neuron, the learning gain degree Lg, corresponding to the modulation gain ratio, increases with increasing the learning cycle, and it saturates at about the 300th cycle. By varying pc from pc*, we find that a plot of saturated learning gain degree Lg* versus pc forms a bell-shaped curve with a peak at pc* (where the diversity degree in spiking patterns of GR cells is also maximum). Consequently, the more diverse in recoding of GR cells, the more effective in motor learning for the OKR adaptation.

Key Words: Optokinetic response, Cerebellar ring network, Diverse recoding, Effective long-term depression, Effective motor learning

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Cloud-based KBrain-map platform for 3D reconstruction and visualization of neurons from terabyte-scale data

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In the field of connectome research, there is an ongoing need for analytical techniques to process the massive data obtained by the imaging technologies using high-resolution microscope.
In this study, we propose pre-computed pipeline and methodology generating an automated data set and providing an advantage of block storage in a cloud environment, which are eventually utilized the images produced by electronic microscopy (EM) to be visualized and analyzed in three dimensions through a web browser, KBrain-map platform.
We implemented the open sources and computer vision libraries in this pipeline to detect neurons, synaptic connectivity, and neural structure in terabyte-scale EM data. This platform includes an automated pre-processing pipeline for EM images with high-capacity storage space. In addition, we developed the KNeuroViz, an analytical solution for post-processing, for web-based 3D visualization and analysis of neurons. This solution is a modified software of Neuroglancer and optimized to the web-based system. This will be implanted into KBrain-map platform, eventually.
In current study, we propose the KBrain-map platform which is a cloud-based platform and includes the pipeline to visualize neurons and synapses in 3D and analyze their connectivity, efficiently. This system will be continuously integrated with various analysis modules providing an interactive platform for brain research.

Key Words: Distributed computing, Neuroimaging, 3D visualization and client/server, Electron microscopy, Segmentation

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APPswe Organoids generated in a PDMS insert culture system (PICS) recapitulate Alzheimer's disease pathology2

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Brain organoids, derived from human induced pluripotent stem cells (iPSCs), provide a platform for studying the early developmental stage of human brain and mechanisms underlying brain disorders related to abnormal brain development such as autism in vitro. Brain organoids from Alzheimer's disease (AD) patients' derived iPSC have shown to recapitulate AD-associated pathology including extracellular amyloid-β(Aβ) accumulation and hyperphosphorylation, however, long-term culture of brain organoids in the current methods have some shortcomings such as sticking together, which leads to loss of organoids and inconsistent results. To overcome this issue, producing more organoids is required, which implies that researchers have to spend more time and cost. Alternatively, we can culture brain organoids on 12-well plate. But it is more labor intensive to change media for each well than current 100 mm-dish or bioreactor culture methods, and heterogeneity between organoids cultured in different well has been reported. Here, we developed a new culture platform for brain organoids by adding an insert made of Polydimethylsiloxane (PDMS) in a 100 mm-dish. This PDMS insert culture system (PICS) prevents organoids from sticking to each other by dividing the sections of the plate but allows culture media to flow through the channels. We are now applying this platform to 2 months culture of organoids carrying the Swedish mutation in the gene coding amyloid precursor protein (APPswe) and will address whether the hallmarks of AD are nicely recapitulated in every organoids in a homogeneous manner We believe that our insert culture system for brain organoids will provide the chance to reduce time and cost and produce consistent data.

Key Words: Organoid, Insert, Culture system, PDMS, APP swedish