

ABSTRACT:
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Excitatory synapses in a given pathway can display significant molecular heterogeneity, but whether that is accompanied by differences in the topographical distribution of parent pyramidal neurons remains unclear. Synaptic vesicle zinc and the zinc transporter ZnT3 are found presynaptically in only half of axospinous synapses in the CA1 hippocampus, suggesting the interesting possibility that different subsets of CA3 pyramidal neurons may give rise to different projections to CA1. To this end, ZN(+) neurons were mapped using retrograde tracing of selenite, whereas miniruby or cholera toxin were used to map the entire neuronal population projecting to CA1. Injections of miniruby or CT confined to the dorsal CA1 region resulted in labeling of neurons across all three CA3 subfields (i.e. a, b, c), as well as in CA2. In contrast, CA1 injections of selenite mostly labeled neurons in CA3b-c, with very few cells found in CA3a, and none in CA2. Quantitative analysis confirmed the different contribution of CA3/2 subfields to CA1 projections when using selenite or miniruby. Thus, ZN(+) and ZN(-) boutons of CA1 axospinous synapses largely arise from two non-overlapping populations of pyramidal neurons that are distinctly organized in a proximo-distal gradient along CA3 and CA2 regions.

In mammals, X-linked gene expression is adjusted by regulatory mechanisms to compensate for the evolutionary loss of Y-linked genes- upregulation of the active X in both sexes and X inactivation in females. A number of genes escape dosage compensation, potentially leading to expression differences between males and females. A comprehensive analysis of more than 4000 sexed expression arrays in 65 human tissues showed a male bias in pseudoautosomal gene expression and a female bias for other genes that escape X inactivation. Sex-specific bias was particularly pronounced in the gyrus and cortex regions of the brain, adipose and gastrointestinal tissues, muscle and heart, different types of immune cells and reproductive organs. For a subset of genes, modulations of dosage compensation mechanisms unique to the sex chromosomes cause sex differences in particular tissues. We propose that escape from X inactivation in human provides females with unique genetic advantages in specific tissue types.

BrainInfo/NeuroMaps online 3D brain atlas: an image publication tool for mouse and macaque data

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Most images of data mapped to brain regions and published in the neuroscience literature do not provide an adequate context for quantitative comparison with new findings. Differences in plane of section, distortion due to floating and mounting sections, and individual anatomical differences all contribute to the problem. We wanted a 3-dimensional brain atlas to which any investigator with access to the Web can map data, retrieve images suitable for publication, and make comparisons with other data mapped to the same atlas.

NeuroMaps provides: (1) a platform for the preparation of neuroanatomical images for publication, and (2) a common database for the storage and display of image data sets in online, three-dimensional 'template atlases' of the macaque and Waxholm mouse brains. The NeuroMaps environment provides: (3) a high-resolution MRI for comparison with experimental data, and (4) detailed, three-dimensionally smoothed outlines of a comprehensive set of macaque brain structures, mapped to the MRI, that can be incorporated into data images for publication.

NeuroMaps accommodates both area data (such as lesion sites or areas of gene expression) and point data (such as recording sites or labeled cells). It provides tools to display and analyze a dataset in a normalized form, in equally spaced coronal, axial, or parasagittal sections. Tools are available: (1) to compensate for a non-standard angle of section; (2) to warp data images by mapping to landmarks in either the hi-resolution MRI or in a segmented template image of the same cross-section; (3) to interpolate to construct missing intermediate sections; and (4) to extrapolate to provide endcaps at the extremities of a region of interest.

NeuroMaps can be used both to prepare individual illustrations of anatomical data in 3D context, and to preserve entire datasets in a form that allows comparison and quantitative analysis of data from a variety of experimental sources. Data images, with approval of the author and the atlas curator, become available over the Web to other users as atlas 'overlays'. These and other tools facilitate the comparison of image data from many sources and the storage of far more image data than can be made accessible in conventional journal publications.

This work has been supported by grants to the University of Washington from NIH Grants MH084791, LM008247, MH069259, RR00166.

2009 SFN Control/Tracking Number: 2009-S-9617-SfN

6-491 486 coronal
91-436 346 horizontal
65-255 191 sagittal

The **body** of your abstract should be no more than 2,300 characters, including punctuation (not spaces). We recommend aiming for this range as a frame of reference, then counting characters and revising accordingly.

2010 SFN Control/Tracking Number: 2010-S-7432-SfN

Title: "Deciphering the Neuronal Circuit Underlying the Anorexia Produced by Ablation of AgRP Neurons"

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Abstract

Background: Ablation of inhibitory neurons that produce AgRP, NPY and GABA in the arcuate nucleus (ARC) of adult mice results in Fos induction in post-synaptic targets of AgRP neurons and starvation within 6 days. We are exploring the critical neural pathways and associated signaling molecules underlying this process.

Primary observations:

1. Chronic subcutaneous delivery of bretazenil (a GABAA receptor partial agonist) maintains feeding and survival following ablation of AgRP neurons, an effect that persists following cessation of drug delivery.
2. Direct delivery of bretazenil into the parabrachial nucleus (PBN), a nucleus that relays gustatory and visceral sensory information, is sufficient to maintain feeding after AgRP neuron ablation, whereas delivery into other post-synaptic targets of AgRP neurons is ineffective.
3. Suppression of serotonergic signaling in the nucleus tractus solitaries (NTS) but not the PBN through chronic delivery of ondansetron (a 5-HT₃ receptor antagonist) protects against starvation.
4. Targeted deletion of serotonergic signaling in the rNTS attenuates anorectic response in AgRP neuron-ablated animals.
5. Pretreatment of lithium chloride, which mimics nausea, prior to ablation of AgRP neurons prevents anorexia in mice after acute ablation of AgRP neurons

Conclusion:

Suppression of PBN activity by bretazenil or ondansetron prior to AgRP neuron ablation, or initiating adaptive process by pretreatment with LiCl can suppress anorexia elicited by acute ablation of AgRP neurons.

Columnar organization of primary visual cortex for fine discrimination

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Cortical representation of sensory information has been extensively studied by finding the stimulus to which a neuron responds best and mapping the progression of this “preferred” stimulus across and through the cortex. This approach has revealed orderly columnar representation of salient sensory features in the form of “stimulus preference maps” or “feature maps” in much of the mammalian sensory cortex. Consequently, such maps are considered to be direct encoders of sensory stimuli but the intrinsic functional value of ordering neurons into maps remains controversial. We report that neurons in the primary visual cortex (V1) are arranged as a columnar map of their optimally discriminable orientations. In contrast to orientation preference maps, neighboring neurons in this map do not necessarily prefer similar orientations but can co-operatively enhance the precision of fine discriminations about the same reference orientation. This map of fine discrimination information arises from a systematic ordering of neurons by their overall orientation tuning characteristic, not simply by their preferred orientations. Our results show that area V1 contains distinct maps of decision-related information for the perception (detection, identification, recognition) and discrimination of oriented stimuli. This organization can facilitate fast and dynamic computing of multiple forms of visually-guided behavior.

Yves JOSSIN PhD

Rap1-Cadherin signaling triggers polarized migration of neocortical neurons

Glial-guided neuronal migration is important for the lamination of the mammalian cerebral cortex. Neural stem cells divide at the ventricular zone (VZ) to produce post-mitotic neurons and progenitor cells. Post-mitotic neurons become multipolar cells at the intermediate zone (IZ) and need to re-polarize towards the cortical plate (CP) before invading it. The signals and mechanisms regulating this polarization are poorly understood.

Members of the Rap sub-family of Ras GTPases (Rap1A, B; Rap2A, B, C) regulate polarization of several cell types. Here we report that Rap activity allows multipolar neurons to initiate their polarization towards the cortical plate and the subsequent transition from multipolar to bipolar morphology. These processes requires Rap's downstream effectors Ral, Rac1 and Cdc42. Down-regulating Rap inhibits polarization but does not interfere with motility of bipolar cells in vivo or in vitro.

Signaling through Rap1 has been implicated in both integrin-mediated and cadherin mediated adhesion events. The role of Integrins in glial-guided migration is controversial. This led us to investigate the involvement of cadherins in neuronal polarization. Classic cadherins are transmembrane proteins that form calcium-dependent homophilic complexes between adjacent cells. In general, cadherins stabilize tissue architecture and are down-regulated in migratory cells. Here we report an unexpected requirement for neural cadherin (NCad) in polarizing migrating neurons that give rise to the neocortex. Maintaining surface NCad requires Rap activity. These findings suggest that N-cadherin induces cell polarization under tight regulation by Rap and its effectors Ral, Rac1 and Cdc42.

John Morris

Characterization of human hippocampus by gene expression patterns

The anatomy of the rodent hippocampus has become increasingly resolved using gene expression (Thompson et al. 2008, Dong et al., 2009), whereas the molecular architecture of the human hippocampus is still relatively unknown. In order to reveal the human hippocampus in greater detail, we generated a dataset at the cellular level using ISH probes for 55 genes. Members of GABAergic (24) and glutamatergic (31) gene families, including known synaptic enzymes, transporters, and receptors, were selected to label a wide range of cell populations. We present comparisons between the rodent and human hippocampus for these genes (along with a subset of 6 genes applied to Macaque hippocampus) that highlight similarities and differences in gene expression across species. Results indicate gene expression may allow for additional parcellation of the human hippocampus into functional domains much like that for rodent. Additionally, stark differences between species suggest an influence of genetic background on gene expression, but will require additional work to demonstrate.

Abstract:

Consolidation of hippocampus dependent memory is dependent on activation of the cAMP/ Erk/MAPK signal transduction pathway in the hippocampus. Recently, we discovered that adenylyl cyclase and MAPK activities undergo a circadian oscillation in the hippocampus and that inhibition of this oscillation pharmacologically or genetically impairs contextual memory. This suggests the interesting possibility that the persistence of hippocampus-dependent memory depends upon the reactivation of MAPK in the hippocampus during the circadian cycle. A key unanswered question is whether the circadian oscillation of this signaling pathway is intrinsic to the hippocampus or is driven by the master circadian clock in the suprachiasmatic nucleus (SCN). To address this question, we ablated the SCN of mice by electrolytic lesion and examined hippocampus-dependent memory as well as adenylyl cyclase and MAPK activities. Electrolytic lesion of the SCN two days after training for contextual fear memory reduced contextual memory measured two weeks after training indicating that maintenance of contextual memory depends on the SCN. Spatial memory was also compromised in SCN-lesioned mice. Furthermore, the circadian oscillation of adenylyl cyclase and MAPK activities in the hippocampus was destroyed by lesioning of the SCN. These data suggest that hippocampus-dependent long-term memory is dependent on the SCN-controlled oscillation of the adenylyl cyclase/MAPK pathway in the hippocampus.