region of NCAM (NCAM-EC) have been linked to schizophrenia, and NrCAM has been proposed as a candidate gene for autism susceptibility. In the present study, we evaluated a transgenic mouse line with elevated NCAM-EC expression for impaired working memory and changes in social approach, relevant to the schizophrenia behavioral phenotype. In addition, we assessed NrCAM null mutant mice for social approach and reversal learning in the Morris water maze, as endophenotypes for the social deficits, repetitive behavior, and cognitive rigidity characteristic of autism. Assays for anxiety-like behavior in an elevated plus maze and open field, and olfactory ability in a buried food test, were conducted to provide control measures for the interpretation of results. In comparison to wildtype mice, NCAM-EC mutants had impaired performance in a delayed non-matching-to-sample T-maze test for working memory. NrCAM null mutant mice had significantly decreased sociability in a three-chambered choice task, whereas NCAM-EC mice showed normal social approach. In addition, deficits in reversal learning were observed in two separate cohorts of NrCAM null mutant mice following acquisition in the water maze task. These results provide evidence that specific cell adhesion molecules mediate domains of function relevant to neuropsychiatric disorders in humans.

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Poster

817. Axon Growth and Guidance: Others

Time: Wednesday, November 19, 2008, 1:00 pm - 5:00 pm

Program#/Poster#: 817.9/A28

Topic: A.04.h. Axon growth and guidance: Other

Title: An optimum principle predicts skewed and heavy-tailed distributions of axon diameters in white matter fascicles

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Abstract: The axon diameter distribution (ADD) has traditionally been measured by electron microscopy (EM) of excised nerve fascicles (Wang et al, J. Nsci, 2008). Recently, it was shown that diffusion MRI can also be used to measure the ADD of myelinated axons in rat corpus callosum in vivo (Barazany et al, ISMRM, 2008). Both methods result in an ADD that is significantly skewed and/or heavy-tailed, resembling gamma and log-normal distributions. Similar size distributions are often observed in nature, but the physical processes that give rise to them (e.g. fragmentation) do not apply to axon development, where the diameter of individual

axons is independently controlled. In this work, we postulate and explore the hypothesis that the observed ADD results adaptively by optimizing the process of information transfer in a spike train given volumetric, metabolic and other constraints. This adaptation can occur either evolutionarily or as a result of development/functioning of individual axons. In this pilot study we explore this hypothesis using the calculus of variations to find the optimal ADD given the constraints of fixed total number of fibers and/or a fixed total cross-sectional area of a fascicle. Other constraints, e.g. limited metabolic activity, can easily be incorporated within the same mathematical framework. More elaborate models can also include the latency between different brain regions in which case well-known relationships between conduction velocity and axon diameter can be used (Gasser and Grundfest, Am J Physiol 1939; Hursh, Am J Physiol, 1939; Tasaki et al., Japan J Med Sci Biophys, 1944). Presently, we use only a single diameter parameter from which we calculate the "inner" and "outer" axon diameters using known scaling relationships (Hursh, Am. Phys. Soc. 1939). We also assume that the relationship between the maximal firing rate and the diameter of individual axons is a simple polynomial. The optimal solution belongs to a new family of skewed and heavy-tailed distributions of which the gamma distribution is a special case, while the log-normal distribution is satisfied only approximately. To our knowledge, no other works have attempted to explain the phenomenologically observed ADD. Here we propose a rationale for these distributions based on physical and physiological considerations.

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Poster

817. Axon Growth and Guidance: Others

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Program#/Poster#: 817.10/A29

Topic: A.04.h. Axon growth and guidance: Other

Title: Numerical modeling of sensory neuron morphogenesis

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Abstract: It is not known what growth, branching or pruning rates will optimize targeting of sensory neurons in future regenerative therapies. For example, large amounts of NGF may promote growth, but may also exhaust neurite resources before a growth cone can reach a distant target. To quantitatively analyze and optimize targeting strategies, we have developed side-by-side in
silico and in vitro studies of neuron growth, branching and pruning using chick DRG neurons as