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Presentation Abstract

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Presentation Title: Imaging metal distribution in Williams syndrome spatially and across time: From cultured cells to postmortem brain tissue

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Authors: ***E. L. OHAYON**^{1,2}, T. CHAILANGKARN³, A. R. MUOTRI³, P. V. CHU², A. R. MUNOZ², U. BELLUGI⁴, T. J. SEJNOWSKI¹, A. LAM²;¹Computat. Neurobio. Lab., The Salk Inst., La Jolla, CA; ²Green Neurosci. Lab., NeuroInx Res. Inst., San Diego, CA;³UCSD, La Jolla, CA; ⁴Lab. for Cognitive Neurosci., Salk Inst. for Biol. Studies, La Jolla, CA

Abstract: Metals play a central role in brain structure, function and health. However, little is known about the changes in their colocalization during development and across scales. This study uses synchrotron-based x-ray fluorescence (SXRF) imaging and computational techniques to examine the role of brain metals and network structure in cognition. In particular, we examine the colocalization of metals in Williams syndrome (WS), a condition with unique social cognitive characteristics, using postmortem tissue and cell cultures imaged at the Stanford Synchrotron Radiation Lightsource. Initially, we compared metal distribution in postmortem samples from WS and typically developing (TD) individuals at imaged at scales ranging from entire hemispheres to local circuits. We demonstrated that SXRF could colocalize and quantify metals in tissue sections as thin as 50 μ m and resolutions as high as 1 μ m. There was strong correlation between distribution of Fe and Zn in subcortical brain structures, white and grey matter, as well as differences corresponding to variations in cell density. However, key questions remain as to how to bridge these observations with function and behavior. The availability of cell cultures of induced pluripotent stem cells (iPSCs), neural progenitor cells (NPCs) and neurons enables the novel examination of metal profiles in individual cells and cellular networks as they develop. To this end, we have begun to test the feasibility of imaging such cultures with SXRF. Primary cultures of somatic cells were grown from dental pulp of exfoliated deciduous teeth from TD and WS individuals. Cell aggregates were expanded as single- and multi-layered cultures on metal-free coverslips. Preliminary SXRF results showed a significant increase in metal uptake, particularly Fe, in both single- and multi-layered cultures as compared to culture media-only slides. No differences were seen between WS and TD at the 10 μ m resolution in the early stages of proliferation (up to 1 week). Experiments are underway to examine both higher resolution and later stages of development of derived iPSCs, NPCs and neurons. These ongoing studies seek to establish whether (i) subtle changes in metal distribution occur in neural cell development and (ii) whether features seen in the postmortem tissue will be reflected in metal distribution in cultures as they form functional networks. Using computational models, we also demonstrate how these changes in brain structure and density can modulate neural activity propagation. We thus begin to bridge the multiscale aspects of brain structure, elemental composition and activity using a unified approach of imaging metal involvement in the brain.

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IMAGING

COMPUTATIONAL MODEL

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