Developmental delay in brain provides clue to sensory hypersensitivity in autism

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New research provides insight into why fragile X syndrome, the most common known cause of autism and mental retardation, is associated with an extreme hypersensitivity to sounds, touch, smells, and visual stimuli that causes sensory overload and results in social withdrawal, hyperarousal, and anxiety. The study, published by Cell Press in the February 11 issue of the journal *Neuron*, uncovers a previously unknown developmental delay in a critical brain circuit that processes sensory information in a mouse model of fragile X syndrome.

Fragile X syndrome is caused by a mutation that interferes with production of fragile X mental retardation protein (FMRP). FMRP has been shown to play a key role in neuronal development and plasticity, and the loss of FMRP results in the complex and severely debilitating symptoms associated with fragile X syndrome.

"A central feature of fragile X syndrome is an alteration in sensory processing that manifests in early infancy and progressively worsens through childhood," explains senior study author, Dr. Anis Contractor from the Department of Physiology at the Northwestern Feinberg School of Medicine in Chicago. "Little is known about how disruptions in the part of the brain that process sensory information, called the sensory cortex, contribute to these deficits."

Dr. Contractor and colleagues used a mouse model of fragile X syndrome that exhibits hypersensitivity to sensory stimuli, similar to the human syndrome, to examine the development of synapses in the sensory cortex. Synapses are the sites of communication between neurons, and the ability of the brain to correctly process incoming information is predicated on the correct development of these structures. Although previous work had shown that there are clear defects in the size, shape, and number of synapses in the sensory cortex of fragile X mice, it was not clear whether the abnormalities had any functional impact on the development of the sensory cortex.

During perinatal development in the normal mouse, there is an activity-dependent maturation of synapses. This sensory-driven maturation of key synapses must occur at the right time, called the "critical period." The researchers found that the fragile X mice exhibited a profoundly altered development of synapses in the part of the mouse cortex that processes sensory information from the whiskers. Loss of FMRP resulted in a dysregulation of synapse maturation so that there was a delay in the normal window for synaptic plasticity.

"The precise timing of critical periods during cortical development is essential for the proper organization of synaptic connections and circuits," says Dr. Contractor. "The delayed timing of plasticity windows we observed might contribute to the altered refinement of cortical circuits that persist throughout the life of the animal and contribute to sensory processing deficits in fragile X syndrome."

More information: Harlow et al.: “Critical Period Plasticity Is Disrupted in the Barrel Cortex of Fmr1 Knockout Mice.” Publishing in Neuron 65, 385-398, February 11, 2010. DOI 10.1016/j.neuron.2010.01.024

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