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Hard of Listening: Auditory Cortex Pathology in Schizophrenia (Stereologically (Un?) Informed Studies of Auditory Cortex in Schizophrenia)

It has long been known that impaired auditory sensory processing and impaired auditory physiology are present in subjects with schizophrenia. An ongoing debate regarding these *in vivo* sensory impairments found within individuals with schizophrenia was whether they might arise solely from impairments in “higher order” brain regions that lead to failed sensory processing (top down impairments), or whether primary deficits in sensory processing may make independent contributions to deficits (bottom up impairments). To resolve this issue, my lab undertook a series of studies to directly examine structural and molecular pathology in this brain region in individuals with schizophrenia. In a series of studies conducted using both biased designs and design-based stereology, we have identified reductions in density and number of dendritic spines in primary auditory cortex in several independent cohorts and have confirmed that this is due to reduction in only the smallest spines. Importantly, these impairments did not result from neuron loss in primary auditory cortex, nor were they recapitulated by long-term antipsychotic exposure in an animal model. These studies have further identified alterations in MAP2 protein that may serve as a common downstream hub for auditory cortex impairments of dendritic morphology. These findings have strongly impacted the field of schizophrenia neuroscience. Our demonstration of cellular and molecular pathology within primary sensory cortex firmly excluded a monolithic “top down” viewpoint. It is no longer tenable to argue that sensory impairments in this illness arise in the absence of sensory system pathology.