Sensory experience plays a critical role in shaping the connectivity and function of the central nervous system. These processes are mediated in part by the action of a program of neuronal activity-driven gene expression. Our investigation of these gene expression programs has uncovered important roles in dendritic growth, the development of excitatory and inhibitory synapses, the composition of protein complexes at pre- and post-synaptic sites, and the production of neuropeptides that control neural circuit development and plasticity. Moreover, defects in the activity-dependent gene program contribute to disorders of human cognition. Thus, our study of this transcriptional response promises new insights into neuronal plasticity and disease.