

Times of dramatic progress in brain research have often been correlated with the development of new and powerful techniques that have changed the kinds of questions one can ask. An historical example may illustrate the point. More than 50 years ago, Nissl studies (Ferraro, 1928) showed that extensive forebrain lesions resulted in chromatolysis and cell loss in the substantia nigra; thus, it was suggested that the substantia nigra gave rise to projections into the basal forebrain. In the late 1950s, another clue emerged, this time linking observations from the field of neuropathology with a discovery in experimental neuropharmacology (Carlsson, 1959a, b; Ehringer and Hornykiewicz, 1960). It had long been recognized that patients with Parkinson's disease suffered neuronal loss in the substantia nigra and that their symptoms were somehow related to striatal dysfunction. Thus, when fluorescent catecholamine assays were developed and combined with pharmacological and neuropathological studies of Parkinson's disease, the dopaminergic nature of the illness was shown. A bit later, Falck and Hillarp (Falck et al., 1962) developed a fluorescent histochemical method to visualize monoamine-containing cells in the brain; this technique was soon applied to show that the rich dopaminergic terminal field in the striatum derived from neurons in the substantia nigra (Anden et al., 1964). In the following decade, refinements in the histofluorescent method and the development of sensitive silver impregnation methods permitted a detailed light microscopic exploration of the dopaminergic nigrostriatal system.

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