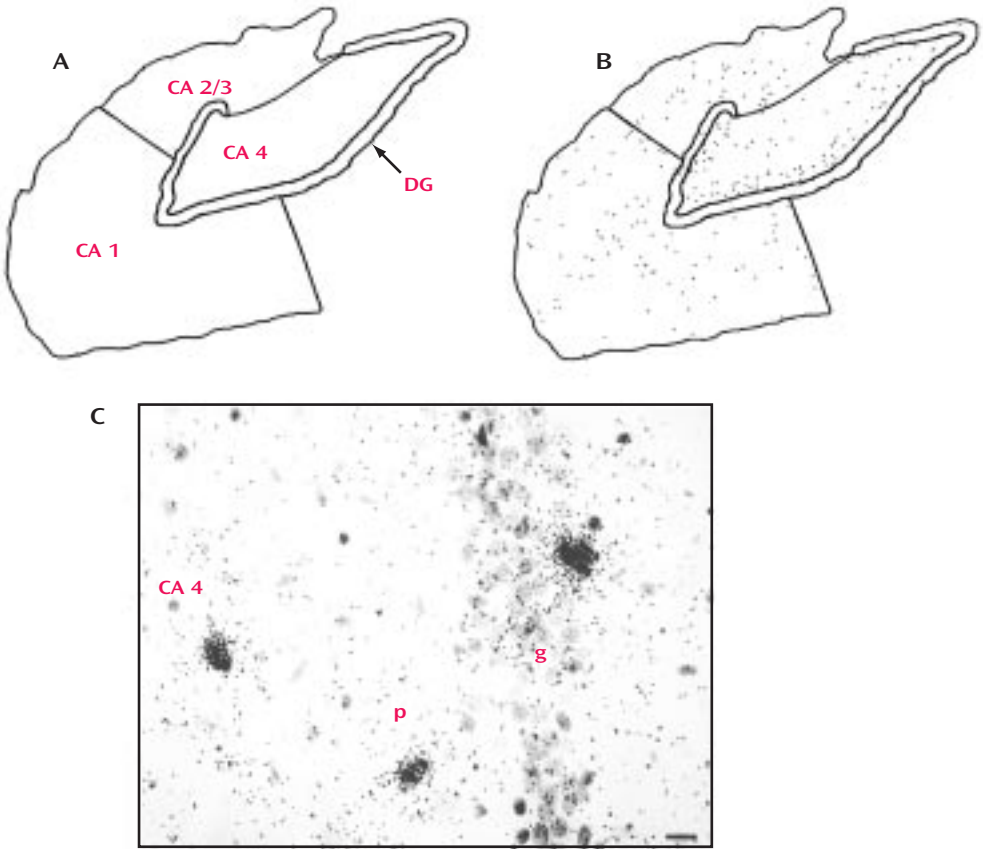
Carol A. Tamminga, M.D., Editor

Hippocampus, III



GABA-Containing Cell Bodies and GAD mRNA

Neuronal signaling in the hippocampus is predominately mediated by excitatory, glutamatergic neurons. Their firing is modulated by a much smaller contingent of γ-aminobutyric acid (GABA)-containing interneurons. The balance between excitatory pyramidal cell firing and GABA-mediated inhibition determines hippocampal function. The rate-limiting enzyme of GABA synthesis is glutamic acid decarboxylase (GAD). Two different genes code for two isoforms of GAD protein found in the human brain, GAD65 and GAD67. The expression of GAD mRNA distinguishes the GABA-containing interneurons from the non-GABA-containing pyramidal neurons.

The figure illustrates the relative density of GAD65 mRNA-positive neurons in the human hippocampus, taken from a comprehensive survey of healthy comparison subjects, patients with schizophrenia, and patients with bipolar disorder. The highest density of GAD mRNA-positive neurons is found in the cornu ammonis (CA) subfield 4. Intermediate levels are seen in CA 2/3 and CA 1, and the lowest levels are seen in the dentate gyrus (DG). The high-power photomicrograph in panel C (taken at a location indicated by the box in panel A) shows three GABA-containing neurons expressing GAD65 mRNA in CA 4 and the polymorph (p) and granule (g) layers of the dentate gyrus. In bipolar disorder patients, GAD mRNA-positive neurons are decreased in number, especially in CA 4, relative to healthy comparison subjects. These results suggest a decreased inhibition of pyramidal neuron activity in distinct regions of the hippocampus in bipolar disorder patients.

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