cells (APCs; dendritic cells) and transported to regional lymph nodes. In the lymph nodes, naïve B cells exposed to the processed antigens, with cooperation of CD4+ T cells, become antigen-experienced and differentiate into antibody-producing plasma cells. After entering the brain, memory B cells undergo restimulation, antigen-driven affinity maturation, clonal expansion, and differentiation into antibody-producing plasma cells (***C***). The contribution of systemically produced antibodies to the pool of antibodies present in the brain is unclear and may depend on systemic antibody titers and integrity of the blood-brain barrier. Based on experimental models with cultured neurons, the presence of antibodies in the brain may lead to neuronal dysfunction by different mechanisms, including functional blocking of the target antigen ($GABA_BR$ antibodies; ***D***), receptor crosslinking and internalization (NMDAR antibodies; ***E***), and disruption of protein-protein interaction, leading to downstream effects on receptors (LGI1 leading to a decrease of Kv1 potassium channels and AMPAR; ***F***). These mechanisms are influenced by the type of antibodies; for example, whereas IgG1 antibodies frequently crosslink and internalize the target antigen, IgG4 antibodies are less effective at crosslinking the target and more often alter protein-protein interactions. *(Panels D-F J Dalmau: Antibody mediated encephalitis. N Engl J Med 378:840, 2018. Copyright © 2018 Massachusetts Medical Society. Reprinted with permission.)*

Encephalitis with N-*methyl*-D-*aspartate (NMDA) receptor antibodies* usually occurs in young women and children, but men and older patients of both sexes can be affected. The disorder has a characteristic pattern of symptom progression that often includes a prodrome resembling a viral process, followed in a few days by the onset of severe psychiatric symptoms, sleep dysfunction (usually insomnia), reduced verbal output, memory loss, seizures, decreased level of consciousness, abnormal movements (orofacial, limb, and trunk dyskinesias, dystonic postures), autonomic instability, and frequent hypoventilation. Monosymptomatic episodes, such as pure psychosis, occur in about 5% of patients. Clinical relapses occur in 12–24% of patients (12% during the first 2 years after initial presentation). Most patients have intrathecal synthesis of antibodies, likely by infiltrating plasma cells in brain and meninges **(Fig. 94-1*I*)**. In about 65% of patients, the brain MRI is normal; in the other 35%, it shows FLAIR abnormalities that can affect cortical and subcortical regions, usually mild and transient, and rarely the presence of contrast enhancement **(Fig. 94-2*B*)**. The syndrome may be misdiagnosed as a viral or idiopathic encephalitis, neuroleptic