Therapeutic X-irradiation of brain possibly causes cognitive impairment associated with synaptic dysfunction. Drebrin is a postsynaptic actin-binding protein and plays an important role in learning and memory. Interestingly, drebrin decreases transiently in the molecular layer of the dentate gyrus (MLDG) of the hippocampus after X-irradiation in parallel with fear memory impairment. However, the mechanism regulating the drebrin decrease is not clear. Our previous study has shown that activation of N-methyl-D-aspartate (NMDA) receptors induces transient drebrin exodus from dendritic spines. In the present study, we examined whether NMDA receptors relate to X-irradiation-induced drebrin decrease. For\textit{ in vivo} study, 10-week-old male mice, without or with pretreatment with an NMDA receptor antagonist MK801, were exposed to 10 Gy of whole brain X-irradiation and tissues were fixed after 8 hours. For \textit{in vitro} study, we used mouse and rat hippocampal cultured neurons. We found X-irradiation decreased the immunostaining intensity of drebrin in MLDG and the number of doublecortin-positive neurons in dentate gyrus. MK801 inhibited the decrease of drebrin immunostaining intensity, but not the decrease of doublecortin-positive neurons. There were no differences in the immunostaining intensity of PSD-95 between sham and X-irradiated groups. Immunocytochemical analysis \textit{in vitro} showed that drebrin cluster density along dendrites significantly decreased 8 hours after X-irradiation. This decrease was blocked by pretreatment with APV. Drebrin cluster density did not decrease after X-irradiation when the proliferation of glial cells was not inhibited. Thus, the present study indicates that NMDA receptor activation mediates X-irradiation-induced drebrin decrease possibly via drebrin exodus and that glial cells may take part in the activation of NMDA receptors after X-irradiation. In addition, it is suggested that NMDA receptor activation underlies X-irradiation-induced acute transient cognitive impairment.