Role of 5-HT_{1A} receptor in myelin damage caused by maladaptation to stress in mice

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Recent studies reported that human psychiatric disorders display oligodendroglial abnormalities and alterations in oligodendrocyte structure. Our previous studies suggested that 5-HT_{1A} receptor in the hippocampus may be involved in the protection of myelin loss induced by unadaptable excessive stress. In oligodendrocytes, adenomatous polyposis coli (APC) appears at maturation and the onset of myelination. In the present study, we investigated whether 5-HT_{1A} receptor regulate remyelination in unadaptable stress-induced myelin damage. A single exposure to restraint stress for 60 min induced a decrease in head-dipping behavior in the hole-board test. This stress response disappeared in mice that had been exposed to repeated restraint stress for 60 min/day for 14 days. In contrast, repeated exposure to restraint stress for 240 min/day for 14 days did not develop stress adaptation, and still showed a decrease in head-dipping behaviors. Immunohistochemistry analysis revealed that the expression level of APC was decreased in the dentate gyrus of the hippocampus of stress-maladaptive mice. These behavioral and biochemical changes were inhibited by chronic treatment with flesinoxan, a 5-HT_{1A} receptor agonist. The present findings indicate that activation of 5-HT_{1A} receptor may promote remyelination in stress-induced myelin damage.