Involvement of peripheral alpha2A adrenoceptor in the acceleration of gastrointestinal transit and abdominal pain induced by intermittent sleep deprivation

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Alterations in noradrenergic signaling have been implicated in the pathophysiology of irritable bowel syndrome (IBS). We have previously shown that acceleration of gastrointestinal transit (GIT) and brain hypernoradrenergic function in intermittent sleep-deprived mice. On the other hand, acetic acid-induced writhes indicates visceral pain features of IBS model animals. In this study, using mice, we investigated whether intermittent sleep deprivation causes changes in acetic acid-induced writhing and whether the number of writhes and the GIT are improved by administration of the hydrophilic clonidine analogue, ST-91. Mice were deprived of sleep intermittently by the small-platform method (20 h/ day) for 3 days. The intermittent sleep deprivation elicited acceleration of GIT and increase number of writhes were significantly improved by ST-91 treatment. The ID\textsubscript{50} values of ST-91 on the GIT and the writhes and the ileal expression of alpha2A adrenoceptor were decreased in intermittent sleep-deprived mice compared to that in cage-control mice. Moreover, the effects of ST-91 on GIT and writhes in cage-control and intermittent sleep-deprived mice were decreased by the administration of BRL44408, a selective alpha2A adrenoceptor antagonist, and not by the administration of imiloxan, or JP-1302, selective alpha2B and alpha2C adrenoceptor antagonists, respectively. These results suggest that the increase of GIT and writhes induced by intermittent sleep deprivation may serve as a model of diarrhea and visceral pain symptoms in IBS. Further, the onset of these symptoms may be related to the hypofunction of peripheral alpha2A adrenoceptor.