THE FOCAL BRAIN PROTON BEAM IRRADIATION INSULT IN RATS – INDUCED MEMORY DISTURBANCE RELATED CHANGE IN ACETYLCHOLINE RECEPTOR BINDING

Abstract

Cerebral dysfunction is one of the major concerns associated with radiotherapy of brain tumours. However, little is known about the neurochemical basis of brain dysfunction induced by proton irradiation. We here investigated the early consequences of brain damages caused by a proton beam. Brains of male wistar rats were locally irradiated with a 70 MeV proton beam. The irradiation dose was set at level known to produce vascular change followed by necrosis, which appeared the late period after irradiation with 30 Gy. The eight-arm radial maze task in irradiated rats was used. In order to assess the preservation (recall) of memory, the rats that showed the spatial cognition were irradiated. The impairment of the preservation memory was not observed in the irradiated rats compared to the control ones 24 hrs after irradiation. Repeated measures of two-way ANOVA of correct choices and number of errors showed no differences between the control group and 30 Gy irradiated group. In order to assess the acquisition process of memory and working memory for the platform location in the water maze, the task was started on the 24 hrs after irradiation. In the learning task (the acquisition process of memory), there was no difference between the control group and irradiated group in the latency to platform. The rats that memorized the location of the standard position were irradiated, and the impairment of the long-term memory was not observed in the irradiated rats compared to the control ones 24 hrs after irradiation. However, the irradiated rats required a substantially longer time finding out the platform than the control rats when the platform was placed in a non-standard position. From this it follows that a proton dose of 30 Gy impaired the working memory of rats. The function of muscarinic acetylcholine receptors was analyzed by *in vivo* binding assay using radioligand quinuclidinyl benzilate ([^{3}H]QNB). The irradiated rats were intravenously injected with 5.5 MBq of [^{3}H]QNB on the 24 hrs after the irradiation. Autoradiographic studies showed a transitional increase of [^{3}H]QNB *in-vivo* binding in the early phase after proton irradiation. On the other hand, no change in *in-vitro* [^{3}H]QNB binding was seen in the autoradiogram of brain slices from the irradiated rats. The cerebral blood flow and the histopathological change in the brain appeared at 5 or 6 months after irradiation. These results indicate that the relation between behavioral

impairment caused by radiation is closely related to the early change in the receptor function which could be detected in *in-vivo* conditions.