Development of a new treatment for hyperbilirubinemia induced psychiatric disorders; preclinical study

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【Introduction】It has been reported that hyperbilirubinemia increase the risk of psychiatric disorder including schizophrenia (Miyaoka 2000) though the molecular mechanisms are not yet well understood. Several reports show the Gunn rat, which is an animal model of congenital hyperbilirubinemia, has agitative like behaviors (i,e,. Hayashida 2009). Recently, our research group have reported that risperidone improve agitative like behaviors in Gunn rat. The risperidone strongly antagonized serotonin receptor (5HT2AR). In this study, we investigated serotonin neurotransmission in the Gunn rat.【Methods】It was investigated whether 5HTAR specific antagonist (Ketanserin) injection improve behavioral abnormality in Gunn rats. The amounts of serotonin and its metabolites in the Gunn rat were measured by high performance liquid chromatograph, furthermore, serotonergic neurons in the dorsal raphe nucleus were visualized by immunohistochemistry.【Results】Ketanserin injection improved the hyperactivity and agitation like behaviors in Gunn rats. There were significantly higher serotonin and its metabolite at the frontal cortex in the Gunn rats compared to the control rats. The immunohistochemistry showed that the number of TPH positive cells was increasing in dorsal raphe nucleus of Gunn rats.【Conclusion】The serotonergic dysfunctions in the cortical regions seem to play an important role in hyeprbilirubinaemia associated abnormal behaviors. Our study suggests that intervention with abnormal serotonergic transmission may improve symptom of hyeprbilirubinaemia associated psychosis.