BBB HYPERPERMEABILITY TO SODIUM FLUORESCIN IN HIGH FAT DIET-INDUCED OBESE MICE WITH IMPAIRED GLUCOSE TOLERANCE: A COMPARISON STUDY USING ICR, C57BL/6J, AND DB/DB MICE
Takashi Ohara, Shinya Dohgu, Fuyuko Takata, Tsuyoshi Nishioku, Atsushi Yamauchi, Hideki Shuto and Yasufumi Kataoka
Department of Pharmaceutical Care and Health Sciences, Fukuoka University, Fukuoka 814-0180, Japan

[Purpose] Diabetes mellitus (DM) is associated with microvascular complications and pathological changes in the blood-brain barrier (BBB) function. Many of the studies on diabetes-related pathophysiology of the BBB have used the diabetic rodent model induced by streptozotocin. There are few BBB studies using experimental model of type 2 DM, a common type of DM. The aim of this study was to test whether type 2 DM causes BBB dysfunction using high fat diet-fed mice and db/db mice, a widely used genetic model of type 2 DM. [Methods] Male ICR and C57BL/6J mice at 4 weeks old were used. Mice divided into two groups were supplied for the special feeding schedule with free access to water, under which the amounts of normal diet or high fat diet (HFD) were restricted (ICR; 3 g/day/mouse, C57BL/6J; 2 g/day/mouse). [Results and Discussion] After feeding for 2 weeks under our schedule, HFD-fed ICR mice exhibited significant increases in fasting glucose and iAUC for glucose compared with those of control diet-fed group. BBB permeability to sodium fluorescein (Na-F) in HFD-fed ICR mice was significantly increased at 2, 4, and 8 weeks of feeding. C57BL/6J mice showed the increases in fasting glucose and iAUC for glucose at 2, 4, and 8 weeks of feeding HFD. A significant increase in BBB permeability to Na-F was observed at 8 weeks of feeding HFD. In contrast, age-matched db/db mice showed no changes in Na-F permeability. [Conclusions] The present findings demonstrated that HFD-induced obesity with impaired glucose tolerance induced BBB hyperpermeability to Na-F. HFD-induced obese mice would be employed as a useful model to investigate pathophysiology of the BBB in type 2 DM.