Serotonin uptake into human cord blood platelets: modulation by maternal metabolic state

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Serotonin (5-HT) plays a crucial role in fetal brain development by regulating the outgrowth of its own neurons and the maturation of their target regions. In adults, active levels of 5-HT in the blood are tightly controlled by the high-affinity uptake of 5-HT into platelets. The aim of the present study was to examine the presence of an analogous 5-HT uptake system in the fetal circulation and investigate its potential modulation by maternal gestational diabetes mellitus (GDM). The study was performed on mother-newborn pairs recruited at the Clinical Hospital Centre Zagreb, Croatia, as a part of our ongoing birth cohort study PlaNS (Placental and Neonatal Serotonin). Cord blood samples were collected via umbilical venipuncture immediately after baby birth. Platelet rich plasma (PRP) was isolated by centrifugation and 5-HT uptake kinetics was studied using a radiotracer-based assay. Mean platelet volumes in whole cord blood and PRP samples were highly correlated, demonstrating that population of platelets isolated in PRP represented well platelets in the whole cord blood samples. Neonatal platelets showed efficient, time- and temperature-dependent 5-HT uptake, with initial rates of specific 5-HT transport saturable over the high-affinity range of 5-HT concentrations (0.1 to 2.0 μM). In all subjects tested, values of Michaelis affinity constant (*Km*) and maximal transport velocity (*Vmax*) were characteristic of the uptake-1 (high-affinity / low-capacity) transport mechanism, and comparable to those in adult platelets. Further, 5-HT transport into cord blood platelets was compromised by maternal GDM, due to decreased substrate affinity (increased *Km* value). In conclusion, data provide the first demonstration of a functional system for 5-HT uptake in human neonatal platelets and suggest that it could represent a potential mechanism mediating the influence of GDM on fetal brain development. The study was funded by the Croatian Science Foundation (IP-2018-01-6547).