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Integrative analysis of epigenetic response to Methamphetamine overdose in rat brain

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Drug addiction is a relapsing disorder resulted from neural adaptations following repeated drug exposure. Methamphetamine (Meth) is one strong central nervous system stimulant that could result in severe addiction. Abuse of Meth is associated with neurologic and psychiatric symptoms and changes in physical appearance, and overdose of Meth use can cause severe brain damage even death. Mounting evidence indicated impaired functions and epigenetic changes of brain structures due to the Meth addiction. However, the reaction of different brain structures to Meth exposure remain largely unclear. In this study, we investigated the transcriptomic and epigenetic response to Meth exposure in four rat brain structures, including Nuclear Accumbent, Dentate Gyrus, Ammon's horn, and Subventricular Zone, which were tightly connect to the reward pathway. By integrating the RNA-seq and ATAC-seq data, we firstly explored the region-specific molecular signatures of across four regions in normal rat brain, and then identified the common and specific features of those four rat brain regions responding to the Meth overdose. These results provided detailed transcriptomic and epigenetic signatures responding to the Meth exposure in different brain regions. This study reveals the different reactions of rat brain affected by abuse of Meth, could providing a better understanding of the addictive process and lead to the potential therapeutic strategies for the prevention and treatment of Meth addiction.