Na\textsuperscript{+}, K\textsuperscript{+}-ATPase dysfunction induces hyperactivity and impulsivity via dopamine D2 receptor activation in mice

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Hyperactivity and impulsivity are usually observed in several psychiatric disorders such as schizophrenia, bipolar disorder, and attention deficit hyperactivity disorder (ADHD). Although changes in Na\textsuperscript{+}, K\textsuperscript{+}-ATPase expression have been observed in the postmortem brain of patients with several psychiatric disorders, underlying neurobiological mechanisms are poorly understood. In this study, we evaluated the effect of intracerebroventricular (ICV) injection of ouabain, an inhibitor of Na\textsuperscript{+}, K\textsuperscript{+}-ATPase, on hyperactivity and impulsivity in mice. Male C57BL/6J mice at 6 weeks old were injected ouabain into the right ventricle under anesthesia. At seven days after ouabain injection, both locomotor activity and cliff avoidance reaction were assessed by using open field test and cliff avoidance test, respectively. Ouabain significantly increased the distance traveled within open field arena as well as exploring behavior, and some mice fell from the edge of cliff avoidance test platform within 10 min. On the other hand, intraperitoneal administration with chlorpromazine and haloperidol, typical antipsychotics which block dopamine D2 receptor, significantly decreased the distance traveled within open field arena as well as exploring behavior in ouabain-injected mice. Noteworthy, we observed significant increase in the number of c-fos-positive cells in the medial prefrontal cortex (mPFC) and nucleus accumbens shell (NAc shell), but not in the ventral tegmental area (VTA) in ouabain-treated mice, which was inhibited by haloperidol. These results suggest that inhibition of Na\textsuperscript{+}, K\textsuperscript{+}-ATPase causes hyperactivity and impulsivity via excessively accelerating dopamine D2 receptor signaling pathway.