1-YIA-29 YIA

Neural mechanisms underlying regulation of motivation for voluntary wheel running in mice

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It is well known that mice rotate running wheels (RWs) persistently without any rewards, reminiscent of behavioral addiction. In the present study, by focusing on this characteristic feature of mice, we investigated neural mechanisms that regulate the motivation for rotating RWs. Individual male C57BL/6J mice were trained to rotate RWs until the number of rotations became stable by giving free access to a RW for 30 min every other day. Subcutaneous injection of a 5-HT_{1A} receptor (5-HT_{1A}R) antagonist WAY100635 (WAY, 1 mg/kg) significantly increased the number of rotations, while a 5-HT_{2A}R antagonist volinanserin (Vol, 0.01 mg/kg) or a 5-HT_{2C}R antagonist SB242084 (SB, 0.3 mg/kg) reduced it. To investigate whether the changes in rotation are caused by changes in locomotor activity, open field test was performed. Although WAY and Vol did not affect locomotor activity, SB increased locomotor activity. These results suggest that the WAY-, Vol-, or SB-induced changes in rotation number of RWs may not be accounted for by the changes in locomotor activity. Taken together, present findings imply that 5-HT_{1A}R-, 5-HT_{2A}R-, and 5-HT_{2C}R-mediated transmission may differently regulate the motivation for rotating RWs in mice and that the latter two might be involved in enhancing the motivation for behavioral addiction.