Nandrolone Increases Aggressive Behavior in Mice: Implications of Glutamatergic Neurotransmission

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INTRODUCTION: In the past few years anabolic androgenic steroids (AAS) has been changed from therapeutic to illicit use. In this context, nandrolone decanoate (ND) is one of the most misuse AAS. Moreover, misuse of AAS induces an aggressive phenotype linked with hyperactivation of glutamatergic system. However, little is known whether ND-induced aggression connects astrocytic glutamate transporter (GLT-1) dysfunction and NMDA glutamate receptor (NMDAr) activity in the brain of mice.

MATERIAL AND METHODS: Here we studied the effects of long-term administration of supratherapeutical ND dose (15 mg/kg/day, up to 18 days, subcutaneous injection) in CF1 adult male mice on aggressive behavior (resident-intruder test). Also, we evaluated glutamate uptake capacity and the immunocontent of GLT-1 in frontotemporal cortex and hippocampus. Besides, we performed in vivo pharmacological management of aggression with memantine (MN, a noncompetitive antagonist of NMDAr) through a single intraperitoneal injection 20mg/kg, 1 hour before resident-intruder test.

RESULTS AND DISCUSSION: We showed that ND significantly enhanced aggression after long-term administration being that at 18th day there were increased in latency and number of attacks. Further, we observed decreased glutamate-uptake capacity along with decreased immunocontent of GLT-1 in hippocampus and frontotemporal cortex, which paralleled with aggressive phenotype. MN abolished ND-induced aggressive behavior.

CONCLUSION: We provided evidences that ND-induced aggressive behavior is mechanistic linked with decreased GLT1 function/expression in frontoparietal cortex and hippocampus leading to increase activation of NMDAr. This reveals the importance of astrocytic glutamate machinery in mediating neuronal mechanisms of aggression.

Keywords: Anabolic-androgenic steroids (AAS), brain, aggressive behavior, NMDAr, glial glutamate transporter (GLT-1).

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