Anabolic androgen steroids induce neurochemical changes in the hippocampus and prefrontal cortex of rat

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Illicit use of anabolic androgenic steroids (AAS) represents a public health problem worldwide (Pope et al., 2014). AAS abuse was first confined to adult athletes and bodybuilders though, recently, it appears to have become widely used among adolescents (see Rainer et al., 2014). AAS are known to cause changes in mood, including depression and aggression (Gruber and Pope 2000; see Rainer et al., 2014). Neurosteroid biosynthesis in corticolimbic neurons is altered following AAS treatment (Agis-Balboa et al., 2009), but the brain circuits and neurons underlying behavioral deficits remain undefined. A number of studies reported that chronic treatment with selective AAS induced modifications of monoaminergic neurotrasmission in different brain regions (Kurling et al., 2005; Tucci et al., 2012; Zotti et al., 2014). Interestingly, Kalinine and colleagues (2014) recently discovered that long-term nandrolone-induced aggressive behavior is associated with decreased extracellular glutamate clearance and NMDA receptors hyperexcitability in the hippocampus of mice. Here, the effect of chronic treatment with AAS on amino acid neurotransmitters release in prefrontal cortex (PFC) and hippocampus (HC), brain areas involved in cognition, learning and memory and aggression (see Kaufman et al., 2015), have been measured using vertical microdialysis in rat. Male Wistar rats were treated with testosterone, nandrolone and stanozolol (5 mg/kg, s.c., n=7-10 for group), or vehicle (propylene glycol, 0.5 ml/kg s.c., n=8) once daily for 4 weeks. Aspartate (Asp), glutamate (Glu), glutamine (Gln), γ-amino butyric acid (GABA) and taurine (Tau) levels were determined by HPLC with fluorimetric detection (Richards et al., 2000). Microdialysis results showed that chronic AAS treatment induced neurochemical changes in amino acids levels in the PFC and HC. Particularly, testosterone significantly increased the levels of Asp, Glu and GABA in the hippocampus but no changes were observed in PFC. Testosterone also increased significantly Tau levels in the cortex. Nandrolone significantly increased the levels of Glu in both cerebral regions, while those of GABA and Tau were increased only in PFC. Conversely stanozolol induced no significant changes in all amino acids levels studied. Interestingly, a combination of nandrolone plus stanazolol induced the most relevant effects. Particularly, we observed a significant increase in extracellular levels of Asp and Glu and a massive decrease of Gln in both brain regions, while those of GABA and Tau were increased only in the cortex.
Despite showing a deep complexity, the present findings confirm that chronic use of AAS affects brain amino acid neurotransmitters concentration in areas of the brain involved in emotional reactivity and aggressive behavior leading to neurochemical modifications likely involved in the central toxic effects observed in abusers.

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