REPEATED EXPOSURE TO COCAINE DURING ADOLESCENCE ALTERS BDNF EXPRESSION AND SIGNALING IN REWARD-RELATED BRAIN REGIONS.

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Modulation of BDNF has been shown to participate in the addictive properties of cocaine (Verheeji et al., 2016). In addition, we have previously shown that developmental exposure to cocaine alters BDNF expression and signaling as a function of long-term abstinence (Giannotti et al., 2014). However, no evidence exists as to how adolescent exposure to cocaine alters BDNF machinery early after the end of treatment. To this end, we have exposed adolescent animals to a repeated cocaine (20 mg/kg) treatment from postnatal day (PND) 28 to PND 42 and sacrificed them 24 hours after the last exposure, i.e. on PND 43. We took advantage of the punching technique, which allows the microdissection of small brain regions such as the VTA, the prelimbic (PL) and infralimbic (IL) portions of the mPFC and the shell and core portions of the NAc, to depict a global picture of the BDNF pathway in the mesocorticolimbic network. We found increased BDNF trkB expression and increased trkB phosphorylation in the VTA with no activation, however, of BDNF-dependent signaling pathways. Notably, in the VTA, the expression of the dopamine transporter was reduced leading to hypothesize an increased dopaminergic tone toward the nucleus accumbens. Accordingly, we found reduced expression and activation of BDNF, trkB and BDNF-mediated pathways in the nucleus accumbens, both shell and core, that could be interpreted, perhaps, as neuroadaptive mechanisms to oppose to VTA activation. In the mPFC, we found differences in the subregional profile of the BDNF system: in the IL, mBDNF protein levels were increased, while trkB expression and phosphorylation were reduced with a concomitant down regulation of BDNF intracellular signaling. Conversely, in the PL, mBDNF proteins levels decreased, with trkB expression and phosphorylation increasing, accompanied by a reduction in BDNF-dependent pathways. Taken together, these results show that, early after a developmental exposure to cocaine, mBDNF expression and signalling are modulated following a specific brain profile. Further, these data suggest that, following developmental cocaine exposure, BDNF is increased early after treatment and not only as consequence of long-term abstinence.