Dependence of accumbens shell dialysate dopamine on the activity of apamin-sensitive slow-conducting Ca\(^{2+}\)-activated K\(^+\) channels

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Introduction: Midbrain dopaminergic neurons have two different firing patterns: single-spike firing, associated with tonic dopamine (DA) release and burst firing, associated with phasic DA release. Burst firing in DA neurons is controlled by apamin-sensitive Ca\(^{2+}\)-activated K\(^+\) (SK) channels. Electrophysiological studies showed that the blockade of SK channels by apamin increases DA burst firing while activation reduces it.

Aim: In order to demonstrate that microdialysis technique is able to detect phasic dopamine release, we evaluated the effect of intra-ventral tegmental area (VTA) administration of apamin on dialysate DA in the nucleus accumbens (NAc) shell and core. In addition we studied the effect of systemic administration of the allosteric activator of SK channels, cyclohexyl-[2-(3,5-dimethyl-pyrazol-1-yl)-6-methyl-pyrimidin-4-yl]-amine (CyPPA) on the increase of dialysate DA in the NAc shell and core induced by systemic raclopride, a pure D\(_2\) antagonist known to activate DA burst firing and to increase dialysate DA in the NAc shell and core.

Materials and methods: By in vivo microdialysis studies we evaluate the effects of apamin (1.7 pmol/1 µl; 3.3 pmol/µl) locally injected into the VTA and the effects of CyPPA (3.3 mg/kg, i.v.) 5 min before the administration of raclopride (75 µg/kg, i.v.).

Results: Intra-VTA apamin, at doses of 1.7 and 3.3 pmol, dose-dependently increased dialysate DA in the NAc shell but not in the NAc core. Doses of 3.3 pmol apamin increased NAc shell dialysate DA by 75% over basal after 40 min, reaching a plateau of 100–125% over basal at 80 min post-drug. CyPPA, given i.v. at a dose of 3.3 mg/kg did not affect basal dialysate DA but reduced to half the maximal increase of NAc shell dialysate DA induced by raclopride (75 µg/kg, i.v.). CyPPA did not affect the increase of dialysate DA induced by raclopride in the NAc core.

Conclusions: Collectively these observations are consistent with the idea that NAc shell dialysate DA can provide a correlate of phasic stimulation of in vivo DA transmission as a result of activation of DA neuron burst firing. Our observations contradict the common belief that brain microdialysis only reflects the tonic modality of DA transmission in vivo.

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