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Pharmacodynamics of the glutamate receptor antagonists in the rat barrel cortex

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Abstract

© 2018 Vinokurova, Zakharov, Lebedeva, Burkhanova, Chernova, Lotfullina, Khazipov and Valeeva. Epipial application is one of the approaches for drug delivery into the cortex. However, passive diffusion of epipially applied drugs through the cortical depth may be slow, and different drug concentrations may be achieved at different rates across the cortical depth. Here, we explored the pharmacodynamics of the inhibitory effects of epipially applied ionotropic glutamate receptor antagonists CNQX and dAPV on sensory-evoked and spontaneous activity across layers of the cortical barrel column in urethane-anesthetized rats. The inhibitory effects of CNQX and dAPV were observed at concentrations that were an order higher than in slices *in vitro*, and they slowly developed from the cortical surface to depth after epipial application. The level of the inhibitory effects also followed the surface-to-depth gradient, with full inhibition of sensory evoked potentials (SEPs) in the supragranular layers and L4 and only partial inhibition in L5 and L6. During epipial CNQX and dAPV application, spontaneous activity and the late component of multiple unit activity (MUA) during sensory-evoked responses were suppressed faster than the short-latency MUA component. Despite complete suppression of SEPs in L4, sensory-evoked short-latency multiunit responses in L4 persisted, and they were suppressed by further addition of lidocaine suggesting that spikes in thalamocortical axons contribute ~20% to early multiunit responses. Epipial CNQX and dAPV also completely suppressed sensory-evoked very fast (~500 Hz) oscillations and spontaneous slow wave activity in L2/3 and L4. However, delta oscillations persisted in L5/6. Thus, CNQX and dAPV exert inhibitory actions on cortical activity during epipial application at much higher concentrations than *in vitro*, and the pharmacodynamics of their inhibitory effects is characterized by the surface-to-depth gradients in the rate of development and the level of inhibition of sensory-evoked and spontaneous cortical activity.

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Keywords

Barrel cortex, Drug delivery, Epipial application, Fast oscillations, Glutamate receptor antagonists, Sensory-evoked potential, Slow wave activity

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