The role of the noradrenergic signaling in the ventral tegmental area in drug craving

The ventral tegmental area (VTA) is a centrolateral part of the A10, the largest group comprising dopaminergic (DA) neurons in mammalian brain. The role of the VTA neuronal activity has been extensively studied in recent decades, particularly focusing on the activity of DAergic neurons, which led to the formation of the reward prediction error model of reinforcement learning. Importantly, phasic DA signaling downstream from the VTA is proposed to underlie drug craving as our recent findings indicate that brief inhibition of the VTA DA neurons is sufficient to attenuate, whereas phasic activation evokes conditional stimulus (CS)-induced drug seeking behavior. The noradrenergic (NA) system is well positioned to control the activity of distinct VTA neuronal populations both at the level of midbrain cell bodies and axon terminals innervating the VTA. Importantly, our recent studies suggest that intra-VTA NAergic signalling might indeed effectively regulate VTA-dependent behavioural functions. Here, we used combination of *in vivo* optogenetics, *in vivo* single-cells recordings, *in vivo* fast scan cyclic voltammetry and brain-region-specific behavioural pharmacology in wild type and tyrosine hydroxylase (Th) transgenic rats (Th-Cre+) to demonstrate functional role of noradrenergic signalling in the VTA in drug seeking behaviour as well as other motivated behaviours. We conclude, that noradrenergic signalling in the VTA, via modulation of phasic DA release in the forebrain, reflect ability of alerting and/or orienting functions, originating from bottom-up information processing to influence CS-induced behaviours, including drug seeking and drug craving.