The role of Locus Coeruleus for sensory processing within mesocortical dopaminergic pathway

Salient events evoke burst-like responses of noradrenergic (NE) neurons of the Locus Coeruleus (LC) and dopaminergic (DA) neurons of the ventral tegmental area (VTA). The associated NE and DA release modulates information processing in the projection targets of LC and VTA. In the rat, terminal fields of both LC-NE and VTA-DA neurons converge in the medial prefrontal cortex (mPFC), a cortical area controlling many cognitive capacities. We investigated the role of LC phasic activation for sensory responses in VTA and mPFC. Under urhetaine anesthesia, noxious stimulation (foot shock, FS) produces a robust short-latency (~20 ms) excitation of LC-NE neurons. In VTA and mPFC, the firing rate modulation induced by FS was present in ~30% of neurons. We classified FS-induced responses of VTA neurons according to latency (early: ~40 ms or late: ~150 ms) and duration (phasic: < 300 ms or sustained: > 300 ms). Similarly, the mPFC single-unit responses differed by latency and/or duration. Suppression of LC ongoing and FS-evoked activity by iontophoretic injection of clonidine, an alpha2-adrenergic receptor agonist, reduced responsiveness in both VTA and mPFC. Population of initially ‘non-responsive’ mPFC neurons showed ‘gating-effect’. Spontaneous discharge of substantial proportion of VTA and mPFC neurons was bidirectionally modulated. These results suggest that depending on the motivational valence of a salient event, LC phasic activation and associated NE release may selectively enhance or suppress signalling within different and, possibly competing mesolimbic and mesocortical pathways. The behavioral data supporting this hypothesis will be presented.