Chapter 11

Acquiring the Excitatory and the Inhibitory Action of Dopamine in the Prefrontal Cortex During Postnatal Development

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11.1 Introduction

Mesocortical dopamine (DA) transmission and its regulation of prefrontal cortical (PFC) firing (also known as persistent activity) have been correlated with several cognitive task-related, decision processes including working memory, reward, and attention (Goldman-Rakic et al., 2000; Horvitz, 2000; Jay, 2003; O’Donnell, 2003). More importantly, it has been proposed that one of the major roles of mesocortical DA is to increase the signal detection ratio by reducing the impact of irrelevant inputs to the PFC. An enhancement of the mesocortical DA signal in the PFC would therefore contribute to optimize cognitive task performance and the response to motivationally salient stimuli (Horvitz, 2000; Cohen et al., 2002; Schultz, 2002; O’Donnell, 2003). We also know that cognitive functions that depend on PFC DA, such as decision making and working memory, do change with the transition to adulthood (Funahashi and Inoue, 2000; Segalowitz and Davies, 2004). They are typically acquired and refined during puberty and late adolescence when widespread structure refinement and functional neuronal maturation occurs in cortical circuits (Giedd et al., 1999; Casey et al., 2000; Spear, 2000; Gogtay et al., 2004). Although the cellular mechanisms underlying this DA-PFC interaction are not fully identified and often contradictory, disruption of this DA modulation has been associated with the characteristic postpubertal/late adolescence emergence of cognitive deficits in schizophrenia (Lipska and Weinberger, 1998, 2000).

In this chapter I will first review recent electrophysiological findings on how DA D1 and D2 receptors influence excitatory and inhibitory neurotransmission in the PFC during the peripubertal transition to adulthood, the cellular mechanism underlying this DA modulation as well as its functional significance. Secondly, I will discuss how a developmental disruption of PFC DA modulation may underlie some of the
11.2 Dopamine-Glutamate Interactions in the Prefrontal Cortex Changes During the Peripubertal Transition to Adulthood

11.2.1 POSTPUBERTAL ENHANCEMENT OF D1 FACILITATION OF NMDA FUNCTION IN THE PREFRONTAL CORTEX

DA modulation of excitatory and inhibitory neurotransmission in the prefrontal Cortex (PFC) undergoes several changes during postnatal development (Benes et al., 2000; Tseng and O’Donnell, 2005a; Tseng and O’Donnell, 2006), probably due to changes that occur at both cellular and subcellular levels during cortical maturation (Spear, 2000; Tarazi and Baldessarini, 2000; Zhu, 2000). Although the cellular mechanisms by which these processes occur are not entirely identified, evidences indicate that DA may facilitate the acquisition of mature cognitive abilities by virtue of a D1-dependent enhancement of NMDA functions in the PFC (Gurden et al., 1999, 2000; Wang and O’Donnell, 2001; Tseng and O’Donnell, 2005a). It is well documented that hippocampal-PFC long-term potentiation (LTP) is enhanced by activation of D1, but not D2, receptors (Gurden et al., 2000). The dependence of LTP on an intact mesocortical projection is evidenced by the lack of LTP formation in animals with DA depletion (Gurden et al., 1999). A role for mesocortical DA on cognitive functioning is further supported by behavioral studies showing that PFC D1 receptors improve memory retrieval and working memory performance (Seamans et al., 1998; Floresco and Phillips, 2001), and D1-NMDA coactivation in the PFC is required for appetitive instrumental learning in adult rats (Baldwin et al., 2002).

At the cellular level, D1-NMDA coactivation can elicit recurrent plateau depolarizations resembling in vivo “UP states” in PFC pyramidal neurons, an effect that becomes evident only after puberty (Tseng and O’Donnell, 2005a). Despite these observations, there is still some debate on whether UP and DOWN transitions are present in awake animals (reviewed by Tseng and O’Donnell, 2005b), evidences indicates that UP states are important cellular elements of information processing, particularly by enabling ensembles of active neurons to synchronize at any given moment (O’Donnell, 2003). UP states or plateau depolarizations could last from a few hundred microseconds and repeat every second under anesthesia and sleep, to several seconds or minutes as observed in the awake state during alert conditions (reviewed by Tseng and O’Donnell, 2005b). Therefore, a D1 facilitation of plateau depolarization in the PFC would provide a temporal window during which context relevant inputs can drive pyramidal neurons into synchronized firing and NMDA-dependent synaptic plasticity would be enabled. Because activation of mesocortical DA is context-dependent and related to attention and salient stimuli (Horvitz, 2000; Cohen et al., 2002; Schultz, 2002), the relevant ongoing activity in the PFC, that is, that mediated by AMPA and NMDA receptors, could become enhanced and reinforced by setting and maintaining a population of pyramidal neurons into the “UP state” via activation of local D1 receptors (O’Donnell, 2003; Tseng and O’Donnell,