Chapter 10
Dynamics of a Neuromodulator – I. The Role of Dopaminergic Signaling in Goal-Directed Behavior

F. Aboitiz

Abstract The mesencephalic dopaminergic system plays a key role in the organization of goal-directed behavior, operating in three different domains: activation of the locomotor system via the dorsal corpus striatum, modulating motivational states and predicting rewards via the nucleus accumbens and amygdala, and planning strategies and monitoring errors via the prefrontal cortex. These operations are based on two modes of dopaminergic signaling. Tonic, longer-lasting dopamine release, and short-latency, phasic, stimulus-related dopamine release (70–100 ms poststimulus latency, less than 200-ms duration). Tonic and phasic release have been associated with distinct signaling systems provided by D1-like and D2-like receptors, respectively. The balance between these two signaling modes modulates the vigor, motivation, and flexibility of goal-directed behavior. I finally present a perspective that attempts to unify the multiple functions exerted by dopamine, in the context of evolutionary theory.

Abbreviations

DA Dopamine
NAc Nucleus accumbens
PFC Prefrontal cortex
RRF Retrorubral fields
SC Superior colliculus

F. Aboitiz
Departamento de Psiquiatría, Centro de Investigaciones Médicas, Pontificia Universidad Católica de Chile, Marcoleta 391, Santiago, Chile, e-mail: faboitiz@uc.cl
**Introduction**

It is now 50 years since the seminal article by Carlsson et al. (1957) reporting that injection of L-dopa rescued reserpine-treated rabbits from their catatonic state. Using the newly developed technique of spectrophotofluorimetry, the researchers found that L-dopa was metabolized into dopamine (DA), which presumably produced the observed behavioral effects. Although highly controversial in its time, this finding earned Carlsson a shared Nobel prize in 2000, not only for discovering DA as a neurotransmitter but also for establishing that neurotransmission in the brain was chemical rather than electrical (Iversen & Iversen, 2007).

More than any other neurotransmitter, research on DA has had a profound impact in the development of modern neuropsychiatry. Its importance in the palliative treatment of Parkinson’s disease, the effects of DA blockers as antipsychotics, the therapeutic effects of stimulants in attention deficit hyperactivity disorder, and the role of the dopaminergic system in addictive disorders testify to its fundamental relevance in behavioral control and in neurological and psychiatric diseases. Subsequent work has unveiled the role of DA as a strong reinforcer in conditioned learning (hence its role in addictive processes; Hyman, Malenka, & Nestler, 2006), but perhaps more importantly as a prediction error signaling system, where the difference between the real and the expected reward determines the error signal and the dopaminergic response, which leads to behavioral plasticity oriented to minimize this difference (Schultz, 2007). Other researchers have pointed out a role of the dopaminergic signal in associating contextual information to unpredicted events, thus facilitating the reinforcement of novel actions (Redgrave & Gurney, 2006). DA also modulates cortical dynamics, and more generally has profound influences on goal-directed behavior, to which cognitive mechanisms appear to be subsidiary mechanisms (see later). Thus, to understand the role of this neurotransmitter in brain dynamics, it is necessary to assess its integrated participation in the different neurobiological and behavioral levels where it acts, both at the cellular and at the systemic levels, and in both subcortical and cortical structures.

In this chapter I will review some key aspects of dopaminergic neurosignaling, with emphasis on the mechanisms of behavioral control during conditioned learning. Furthermore, I will highlight the existence of two different modes of transmission: phasic and tonic signaling, whose appropriate dynamic balance is essential for normal behavior and cognition. Understanding the basics of these processes is fundamental for a thorough discussion of the role of DA in cortical neurodynamics, which will be addressed in Chap. 11. Before delving into these issues, a brief review of the anatomy of the dopaminergic system will be, in my view, of great benefit for the reader.