

as in rats, this structure has a high content of DA but contains very little norepinephrine (3). TH-immunopositive boutons in rat striatum, like those in the primate cortex, are invariably of the symmetric type and their most common targets are dendritic spines, although other axosomatic and axoshaft synapses are also present (26, 27). Moreover, the dendritic spines of the striatonigral projection neurons that receive input from TH-reactive boutons also receive input from an unstained asymmetric synaptic specialization. Freund *et al.* (26) suggested that an important function of DA in the caudate nucleus is to block the spread of excitatory signals at the level of the individual spine. The startling similarity in the targets and mode of termination of DA afferents in the cerebral cortex and caudate nucleus suggest a common principle of synaptic and functional organization in these two anatomically and functionally closely related structures. The similarity is the more impressive as TH boutons do not invariably form symmetric synapses in all brain regions. For example, in rat hippocampus, TH-positive boutons establish exclusively asymmetric synapses on the dendritic spines of hippocampal pyramidal neurons, whereas their contacts on GABAergic nonpyramidal neurons are symmetric (28).

DA Synaptic Complex: Mechanism of Cortical Modulation. The most commonly reported direct effect of DA on the spontaneous activity of prefrontal neurons is inhibition, and this effect can be produced by local microiontophoretic application of DA (29), by systemic administration of DA agonists (30), or by stimulated release consequent to electrical stimulation of the ventral tegmental area (VTA), where the cells of origin of the cortical DA projection lie (31, 32). Indeed, DA release produced by stimulation of brainstem VTA or iontophoretic application of DA can be shown to attenuate the excitatory response of rodent prefrontal neurons to thalamic stimulation (31) or to tail pinch (32). Similarly, DA applied to the prefrontal cortex of monkeys increases the signal-to-noise ratio in single neuronal activity recorded during a behavioral task when the animal was preparing to respond, whereas DA antagonists had the opposite effect (33). It is not known where or how these effects are mediated—i.e., via a direct effect on pyramidal neurons or via interneurons, or both. The present evidence that spines are the targets of symmetric DA-positive boutons and, furthermore, that an asymmetric bouton is also involved may provide some clues. Given that the spines of pyramidal cells in a variety of cortical areas receive a variety of excitatory synapses and can be the site of large EPSPs (34), it would appear that the DA terminal endings on spines are strategically placed within the cortical circuitry to alter local spine responses to excitatory inputs and, through these, make a contribution to the overall excitability of projection neurons in the cortex.

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