

28 - F. GABAergic system

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© SPMM Course C. Serotonergic pathways Most of the brain's serotonergic neurons originate in the midbrain dorsal and median raphe nuclei and ascend to innervate the entire cortex, basal ganglia, thalamus, and also descend to the spinal cord. D. Noradrenergic pathways Noradrenergic projection originates at the locus coeruleus (pons) and ascends to most of the cortex via medial forebrain bundle. Similar to the serotonin system, noradrenergic projections also descend to the spinal cord. E. Glutamatergic system Glutamate is the most common excitatory neurotransmitter in the brain. As a result, almost all cortical descending tracts (from pyramidal cells) rely on glutamate for neurotransmission. This large output of corticofugal fibres makes up most of the corona radiata. All of the association and commissural fibres also use glutamatergic transmission. Many thalamic neurons are also glutamatergic. Thus thalamocortical projections are also glutamatergic. In addition cerebellar output from deep nuclei, subthalamic nuclei to globus pallidus projections, and brainstem to spinal cord projections are also predominantly glutamatergic. F. GABAergic system GABA is the primary inhibitory neurotransmitter in the brain. Unlike other neurotransmitters, there are no specific neurochemical pathways where GABA is dominant. Instead, GABA is the major transmitter for cerebral interneurons that are ubiquitous throughout the cortex. Interneurons are usually short neurons that serve to connect two other neurons, thus forming an essential part of the complex wiring pattern of the cortex. They carry neither motor nor sensory information but serve to modulate local neural circuitry. 2 major cortical interneuron subtypes are noted: parvalbumin (PV)-expressing interneurons (~40% of all interneurons) and somatostatin (SST)-expressing interneurons (30% of interneurons, also called Martinotti cells). A reduction in the expression of PV-interneurons in the frontal cortex is now a well-replicated feature of schizophrenia. PV-interneurons are of 2 subtypes: Basket cells and Chandelier cells. Basket cells receive direct input from thalamocortical projections. They form synapses with the soma or dendrites of the pyramidal neurons and serve to provide the excitatory-inhibitory balance to the cortex. Chandelier cells form synapses with the proximal axonal hillock of pyramidal neurons. They may have an overall excitatory role by serving to short-circuit the action potential propagation though their role is still unclear.

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□ Heide et al. Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. *Brain*. 2013 Jun;136(Pt 6):1692-707.

□ Ruigrok TJ. Cerebellar nuclei: the olivary connection. *Prog Brain Res*. 1997;114:167-92.

□ Lewis DA et al. Cortical parvalbumin interneurons and cognitive dysfunction in schizophrenia. Trends in Neurosciences 2012 Jan;35(1):57-67. □ Andreasen NC et al. "Cognitive dysmetria" as an integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar circuitry? Schizophr Bull. 1998;24(2):203-18.

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