



FIGURE 30-1 Neurobiology of anxiety disorders.

Neurotransmitters

Although other neurotransmitters have also been implicated in the pathophysiology of anxiety disorders, disturbances in serotonin, norepinephrine, and gamma-aminobutyric acid (GABA) appear to be most significant.

Cell bodies of origin for the serotonin pathways lie within the raphe nuclei located in the brain stem. Serotonin is thought to be decreased in anxiety disorders. Cell bodies for norepinephrine originate in the locus ceruleus. Norepinephrine is thought to be increased in anxiety disorders. GABA is the major inhibitory neurotransmitter in the brain. It is involved in the reduction and slowing of cellular activity. It is synthesized from glutamic acid, with vitamin B₆ as a cofactor. It is found in almost every region of the brain. GABA is thought to be decreased in anxiety disorders (allowing for increased cellular excitability).

Areas of the Brain Affected

Areas of the brain affected by anxiety disorders and the symptoms that they mediate include the following:

- Amygdala: Fear. Particularly important in panic and phobic disorders.
- Hippocampus: Associated with memory related to fear responses.
- Locus ceruleus: Arousal
- Brain stem: Respiratory activation; heart rate
- Hypothalamus: Activation of stress response
- Frontal cortex: Cognitive interpretations
- Thalamus: Integration of sensory stimuli
- Basal ganglia: Tremor

Anxiolytic Agents

Action

Side Effects

Benzodiazepines	Increases the affinity of the GABA _A receptor for GABA	Sedation, dizziness, weakness, ataxia, decreased motor performance, dependence, withdrawal
SSRIs	Blocks reuptake of serotonin into the presynaptic nerve terminal, increasing synaptic concentration of serotonin	Nausea, diarrhea, headache, insomnia, somnolence, sexual dysfunction
Noradrenergic agents (e.g., propranolol, clonidine)	Propranolol: blocks beta adrenergic receptor activity Clonidine: stimulates alpha-adrenergic receptors	Propranolol: bradycardia, hypotension, weakness, fatigue, impotence, GI upset, bronchospasm Clonidine: dry mouth, sedation, fatigue, hypotension
Barbiturates	CNS depression. Also produces effects in the hepatic and cardiovascular systems	Somnolence, agitation, confusion, ataxia, dizziness, bradycardia, hypotension, constipation
Bupropion	Partial agonist of 5-HT _{1A} receptor	Dizziness, drowsiness, dry mouth, headache, nervousness, nausea, insomnia