• Understanding neurotransmitters and their actions is helping us understand psychoactive drugs.
• Virtually all psychoactive drugs act at synapses affecting one or more of the steps we just listed.
• For example, the first drug we’ll encounter in our discussion of Parkinson’s disease, L-dopa, affects the first step (synthesis of neurotransmitter).
• L-dopa is a “precursor” or ingredient DA neurons can use to make DA.

2 Categories of Drug Actions
A drug which mimics or somehow increases the effects of a neurotransmitter is called an AGONIST.
A drug which blocks or somehow decreases the effects of a neurotransmitter is called an ANTAGONIST.

Drug Actions

- **AGONIST examples:**
  - Narcotic pain relievers fit and activate opiate receptors mimicking the action of normal endorphins.
  - Nicotine fits into & stimulates ACh receptor sites, arousing the cortex like ACh.

- **ANTAGONIST examples:**
  - Haldol blocks DA receptors in schizos.
  - Naloxone blocks opiate receptors.
  - Atropine blocks muscarinic ACh receptors & curare or botox block nicotinic ACh receptors.

Recall the Basal Ganglia p. 361

- Functions:
  - Learning movement sequences performed as a unit.
  - Initiating those motor programs when needed.
  - Inhibiting undesired movements.

Recall the Basal Ganglia p. 361

Basal Ganglia or “Striatum”
Parkinson’s Disease (362-364)

• About 1-2/100 of those over 60 have PD (about 1,000,000 total in US)
• Symptoms: Difficulty initiating movements, slow movements, loss of balance reflexes, muscle rigidity & tremors-at-rest
• Reduction in movement is also seen in lack of facial expression & blinking; shuffling walk without assoc. arm movements; soft, halting, monotone voice; slow blinks; small writing; feeling stuck or frozen
• Also cognitive slowing & depression in many

What’s Happening in Brain?

• Progressive loss of DA cells in substantia nigra which normally send DA messages to basal ganglia
• We all gradually lose neurons but those with PD may have accelerated loss (70% or more gone)
Possible Causes

- Early Parkinson’s disease – strong genetic link
- (see next slide)
- Environmental toxin of some sort (herbicides, pesticides): IA, MN, ND, SD, & NEB have highest rates in US! Those working with pesticides in California have 3x the risk of PD than the general public.
- Other toxins (carbon monoxide, industrial) also linked to increased risk.

Possible Causes continued

- Head injury may be associated with up to 11 fold increase in risk & earlier age of onset.
- 1 concussive loss of consciousness → 32% increase in risk, several losses of consciousness → 174% increase in risk
- Caffeine or nicotine use may decrease your risk significantly! It appears the neurotransmitter effects of these drugs decrease the impact of neurotoxin exposure.

PD Concordance in Twins

- Early Onset (16 pairs)
  - MZ 100% (4 pairs)
  - DZ 16%
- Late-Onset (161 pairs studied)
  - MZ 13%
  - DZ 16%
- This suggests strong genetic influence in the rare cases of early PD but relatively weak genetic influences on regular PD

Treatments

- Increase DA production with L-dopa
  - Problems: L-dopa induced side effects as dose goes up & loss of effectiveness over time
  - http://www.youtube.com/watch?v=2TU2s3VxEI4
- Stimulate DA receptors with DA agonists that fit the DA receptors

When Drug Therapy Fails

- When drug effectiveness declines, experimental options include:
  - Deep brain stimulation to block hyperactivity in this system
    - http://www.youtube.com/watch?v=atN6JeFjStI
  - http://www.youtube.com/watch?v=VossqQJ12T4
  - DBS means that surgical treatments like pallidotomy; thalamotomy (pretreated if face surgical Lesion are used)
  - DBS also decreases impulse control problems of PD patients
  - Experimental: Transplant of DA producing cells into brain

Parkinson’s Disease

- Another abnormality: Lewy Bodies (abnormal clumps of proteins in neurons)
- May precede the development of PD symptoms
- Lewy bodies found in lower brain stem in REM behavior disorder – 2/3’s of those patients develop PD within 10 yrs
- Also sometimes seen Alzheimer’s disease

Figure 11.21

Another abnormality: Lewy Bodies